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A New Forensic Journal

We welcome to the field of forensic journalism the *Journal* of the Forensic Science Society, which makes its appearance within less than a year of the inaugural meeting of the Society in Nottingham, last year.

The *Journal* is edited by Mr. S. S. Kind and the editorial policy is to make the publication useful, interesting and intelligible to lawyers and police officers, as well as to pathologists, serologists, etc. Indeed, it is anticipated that lawyers and police officers will 'write many of the articles appearing the *Journal.*' The object is, therefore, to make the *Journal* attractive to non-specialists. In this respect it has embarked on the same programme of propaganda and education as that which characterizes the American *Journal of Forensic Sciences.*

The first issue is devoted largely to a symposium on *The Investigation of Fatal Road Accidents.* There is also an original contribution on the *Estimation of Age in Infancy.*

The *Journal* should fulfil a useful and timely need in Great Britain. We congratulate the Editor and the Society on the rapid progress it has made, and wish the new *Journal* a long, successful and productive future.

Modern Blood Group Mythology*

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The medicolegal applications of blood grouping tests to solve problems of disputed parentage and for examining blood and other stains in cases of murder, assault and rape are well known. The numerous pitfalls of these delicate tests have been the subject of a number of previous reports[1,2]. Most errors which have been made can be traced to lack of knowledge and understanding on the part of the investigator, and to lack of objectivity in making observations due to failure to use the blind technique[3].

The field of blood grouping has become so complex, that newcomers to the field must depend on textbooks and monographs when acquiring their basic training. Unfortunately, with only a few outstanding exceptions, the books on the subject presently available are uncritical, each having copied the misinformation they contain from the same single source, which has become a sort of bible on the subject. As a result, the innocent beginner has his mind poisoned by many misconceptions, and it is much more difficult to unlearn the wrong information thus acquired than to learn this difficult subject correctly in the first place. Thus, these errors and misconceptions have become firmly entrenched in the literature and bid fair to become a permanent part of our medical heritage.

The purpose of this paper is to expose this modern blood group mythology, so that the neophyte may be placed on his guard and learn to be critical of the literature, and also to indicate where reliable information is available concerning the problems with which the blood group expert is concerned.

My first experience with blood group mythology occurred 32 years ago when, in my first published article[4], I naively cited a Japanese author who claimed that blood grouping tests were in vogue in China and Japan in the thirteenth century. Dr. Karl Landsteiner then referred me to a book by H. Breitenstein, *Die Gerichtliche Medizin der Chinese*, by Wang-in-Hoai, Leipsig, 1908, Grieben's Verlag, Chapter 15 of which was the source of this myth.[5] In one test described here, the fingers of 2 individuals were punctured and their blood allowed to drop into a basin of water. If their

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blood flowed together they were related; but if the drops of blood flowed apart they were not. In a second test, the blood of a claimant to an estate was allowed to drop onto the skeleton of the deceased; if the blood soaked into the bones he was a true heir, but if it could easily be washed off, his claim was fraudulent. This, then, was blood grouping science in ancient China and Japan.

Since this early experience, I have been careful always to consult the original sources myself, before making any citation of the literature. As a result, I believe that my more than 400 articles and half dozen books on blood grouping are singularly free of misquotations and myths. Unfortunately, the same cannot be said for the publications of certain other workers and, as will now be shown, blood group mythology constitutes a large portion of the current literature of the blood grouping field.

Blood Group and Disease

In July 1960, two leading medical journals, the *Lancet* and the *Annals of Internal Medicine* both contained full length articles perpetrating and perpetuating blood group mythology. The introduction to the article[6] in the *Lancet* asserts:

'During the past decade the association of certain diseases with particular blood groups has been demonstrated. Thus, duodenal ulcer has an association with group O (Race and Sanger, 1958), carcinoma of the stomach, Addisonian anaemia, and salivary gland tumours tend to rise more commonly in group A patients (Aird *et al.*). Duodenal ulcer is relatively commoner in non-secretors . . . (Clarke *et al.*)'.

The authors of the paper[7] in the *Annals of Internal Medicine* conclude, based on 45 cases:

'There is a significant decrease in the frequency of group A blood in Negro women with the accelerated form of hypertension'.

Thus, myths about the association of particular A–B–O blood groups and particular diseases are cited as if they were established facts, and at the same time new myths are created and added to the literature. How did this come about?

This particular line of research was in vogue 30 years ago, as can be seen from my book published in 1943.[8] Such studies, with the exception of the association between blood groups and erythroblastosis fetalis, and the relation of blood group incompatibility to hemolytic transfusion reactions, have no rationale, and lead only to contradictions and fallacies. They therefore were discontinued until a pronouncement by a famous mathematician that 'no gene is neutral in selection' led to their revival. However, mathematics is no substitute for common sense and experience and, as Lancelot Hogben[9] has pointed out on page 27 of his book, there has resulted

'a considerable number of reports written on both sides of the Atlantic by mathematically trained statisticians, which were hardly more than a waste of paper on which they were written'.

A Priori Probabilities. The fallacy in these reports can perhaps be more easily understood from the following hypothetical example. Suppose a coin is tossed 8 times, and that each time 'heads' turn up. The following question is then posed:

'Is this a *fair* coin, or does the coin have *heads* on both its sides?'

This is a problem in what is known as *inverse probabilities* and for an intelligent answer to the question something must be known of the *a priori probabilities*. Thus, two contrasting cases may be visualized. In one case, the coin used for the experiment is selected at random from the change in one's pocket—Knowing, as we do, that the U. S. Mint rarely makes an error, we may then estimate the *a priori* chance of a two-headed coin as only, say, 1 in about 100 million. On the other hand, the chance of 8 heads occurring in succession when tossing a true coin, namely, 1 in 256, is so much greater, that one may still reasonably conclude that the coin was a 'normal' one and that the 8 heads were merely a chance occurrence. In the contrasting case, the coin used for the experiment has been provided by a friend, notorious for his fondness for practical jokes. In that instance, the occurrence of 8 heads in succession would probably be sufficient to convince us that this is another of his practical jokes, and that the coin, like him, is two-faced. Thus, from the identical experimental results opposite conclusions may be drawn depending on the *a priori* probabilities.

As another example closer to the subject under discussion, one may consider the problem of detecting linkage in human heredity. Since it is now believed that human beings have 23 pairs of chromosomes, the *a priori* chance that 2 different genes selected at random, and which are not sex-linked, are on the same chromosome is only about 1 in 22. Therefore, if the results of tests deviate at the 5% level from the expectancy under the '*null hypothesis*' namely, that the genes are not linked, this could hardly be considered sufficient to overcome the *a priori* likelihood that the genes are not linked, especially considering that many linked genes are so far apart on the chromosomes that the rate of crossing-over may not deviate appreciably from 50%, making the detection of linkage impossible. This causes one to regard with askance reports in the literature claiming evidence for linkage between genes for blood factors like $\mathbf{Le^a}$ and $\mathbf{Lu^a}$, especially since the reagents for testing for these factors are so feeble and of such low specificity that reproducible results can be obtained only with considerable difficulty. Aside from the fact that subconscious bias, and the failure to use the '*blind technique*', may lead to faulty observations, one should challenge the conclusions of this investigator,[10] since he makes no allowance for the *a priori* probabilities. That this investigator also claims evidence for additional linkages, namely, between myotonic dystrophy and Lewis blood groups, finger prints and Lewis blood groups, cataract and blood group O, and eye color and Duffy blood groups, etc. is noteworthy. One must conclude that

either this investigator has been remarkably lucky or he is extraordinarily uncritical and gullible. As for the sib pair method of detecting and measuring linkage, the fallacies of such studies have already been discussed elsewhere.[8]

The knowledgeable serologist approaches the study of associations between blood groups and disease with quite a different attitude from that of the mathematician. To the former the *a priori* likelihood of an association appears so small, that he is not impressed by deviations from the 'null hypothesis', even at the .0001 level, while the mathematician who reasons from ignorance draws sweeping conclusions from deviations at the 5% level. However, even the mathematician finds it hard to accept the reports in the literature of an association between blood group A and fractured femur.[11]

This discussion may be terminated by citing a fallacy in inverse probability that was very popular about 50 to 100 years ago. Since our telescopes do not magnify sufficiently, there is no way of knowing whether or not life and animals such as are present on the earth also exist on Venus. Therefore, the chance that there are no cows is one half; the chance that there are neither cows nor goats is $\frac{1}{2} \times \frac{1}{2}$ or $\frac{1}{4}$, and continuing in this way through **n** (a vast number) species, the chance that none is present on Venus is only $\frac{1}{2^n}$, an infinitesimally small number. By *reductio ad absurdum*, it therefore follows that life *must* be present on Venus. However, this or similar mathematical proof will not change the *a priori* convictions of astronomers and biologists who know that conditions on Venus preclude any possibility of life, as we know it on earth.

Bias. For completeness, some mention must be made of the role that subconscious bias has played in coloring the judgment of those workers who have been wasting their time studying the distribution of the A–B–O blood groups in various diseases. An outstanding example is provided by Billington's study[12] on the A–B–O groups in carcinoma of the stomach. When he was unable to confirm the earlier claim[13] that in carcinoma of the stomach, the frequency of group A is increased, Billington subdivided his series of cases according to the location of the lesion, in the cardia, pylorus or body of the stomach, and asserted that he then found that the association held but only for lesions in the body of the stomach. This led Wiener[14] to inquire whether

> 'in assigning the cancer to one or another area, the investigator was subconsciously influenced, in borderline cases by his prior knowledge of the patient's blood group'.

In his response, Billington[15] confessed:

> 'I admit I am unable to exclude the possibility that the figures in relation to the site of gastric carcinoma might have been influenced in borderline cases by knowledge of the patient's blood group . . . An analysis of hospital records by a single interested observor (perforce myself) must always be regarded with suspicion'.

Despite Billington's admission, the mythological association between A–B–O blood and carcinoma of the stomach continues to be cited in reviews by blood group paradoxers.[16] In such reviews, only papers favorable to

their own concepts are cited by blood group mythologists, and no reference is made to other papers[17-20] which contain evidence disclosing the fallacies in their views. One of the earmarks of paradoxers and mythologists is the care with which they avoid any reference to sources which contain evidence revealing the errors in their preconceived ideas, so that it is significant that such references are missing from the book by Race and Sanger.[16]

The claim that has gained widest notoriety is that group O persons are more prone to develop duodenal ulcer than individuals of other blood groups, and it is instructive to examine the kind of evidence on which this claim is based. Pell *et al.*,[38] studied the ABO groups of 12,904 employees at 4 different locations of a plant, among whom were 298 with a history of duodenal ulcer, and 508 with hypertension. They found 44.4% group O among the controls and 49.3% group O among those with ulcer, and concluded that these results were statistically significant at the P = .07 level, and supported the previous claims that group O persons are more susceptible to ulcer. (The present writer's own calculations show the difference to be only 2.5 times the probable error, making P = .09, not .07.) However, they fail to observe that when the distributions of the ABO groups among the controls at the 4 locations are compared, at location 2 the frequency of group O is only 40.4%, the difference from the average here being statistically significant at the P = .02 level. Based on this, one might be justified in speculating that group O persons may have shunned location 2 because a shortage of milk there was a hazard, in view of their predisposition to ulcer, or devise some alternative equally foolish hypothesis. The anxiety of Pell *et al.* to obtain a significant result, and their misguided and biased type of reasoning, is betrayed also by the wording of their conclusions regarding hypertension.

'The findings among hypertensives were inconclusive, but did suggest that persons with type A have a slightly greater chance of developing hypertension than have those with type O.'

If other investigators doing this kind of work reason in the same way, as seems probable, those who do not find the expected excess of group O among persons with duodenal ulcer would not be likely to report their results—only those who get the 'correct' deviation would do so. This is in line with the natural desire to 'get on the band wagon'. Then, by pooling a number of such reports, all with the 'correct' deviation, one would finally obtain a large enough total to make the small deviation 'statistically significant.'

Fisher's Synthesis and Little d

Up to the present time at least 18 different blood factors have been found, belonging to the Rh–Hr system, as shown in Table 1. In 1941, when I found[21] the second Rh–Hr factor, now designated **rh′**, the problem had to

be resolved of the serologic and genetic relationship between this blood factor and the original blood factor of Landsteiner and Wiener, now designated **Rh_0**. Three chief genetic possibilities suggested themselves, namely, independent inheritance (separate chromosomes for the genes determining **Rh_0** and **rh′**, respectively), linkage (separate loci for the genes for **Rh_0** and **rh′**, but on the same chromosome), and multiple alleles. By family and population studies, the possibility of separate loci, either on the same or different chromosomes was ruled out, but the fact that blood which was both **Rh_0** and **rh′** positive had a frequency higher than 50% ruled out the possibility of allelism between genes for these two factors.[8] It then became clear that heredity was by multiple allelic genes,[22] but that the gene products (*agglutinogens*) could have multiple serological attributes (*blood factors*).[23] Thus, each allelic gene determines a corresponding agglutinogen having multiple blood factors inherited together as a block. Wiener predicted that the number of blood factors characterizing any Rh–Hr agglutinogen was theoretically unlimited, and depended largely on one's enterprise and ingenuity in finding antisera of new specificities; he made no attempt, however, to anticipate the nature of the specificity of blood factors still to be found since, as he asserted, this was largely unpredictable. This theory advanced by Wiener in 1942 has stood the test of time and requires no modification in principle, only in detail. In 1943, for example, when only 4 Rh–Hr factors were known, R^1 was defined as a gene determining a corresponding agglutinogen Rh_1 characterized by the blood factors **Rh_0** and **rh′**, but lacking **rh″** and **hr′**. Today, when at least 18 Rh–Hr blood factors are known, the gene presently designated R^1 determines an agglutinogen

Table 1: List of Known Rh–Hr Antibodies and Corresponding Blood Factors

Antibodies	*Blood Factors*	*Antibodies*	*Blood Factors*
1. Anti-rhesus / Anti-**Rh_0**	**Rh_0** and **Rh_0**	10. Anti-**rh^{w_2}**	**rh^{w_2}**
		11. Anti-**rh^G**	**rh^G**
2. Anti-**rh′**	**rh′**	12. Anti-**rh_i**	**rh_i**
3. Anti-**hr′**	**hr′**	13. Anti-**Rh^A**	**Rh^A**
4. Anti-**rh″**	**rh″**	14. Anti-**Rh^B**	**Rh^B**
5. Anti-**hr″**	**hr″**	15. Anti-**Rh^C**	**Rh^C**
6. Anti-**rh^{w_1}**	**rh^{w_1}**	16. Anti-**Rh^D**	**Rh^D**
7. Anti-**hr**	**hr**	17. Anti-**Hr**	**Hr**
8. Anti-**rh^{x_1}**	**rh^{x_1}**	18. Anti-**hr^S**	**hr^S**
9. Anti-**hr^V**	**hr^V**		

Rh_1 having the 11 blood factors **Rh_0**, **rh′**, **rh_i**, **Rh^A**, **Rh^B**, **Rh^C**, **Rh^D**, **rh^G**, **hr″**, **hr^S** and **Hr**, but lacking 7 blood factors **rh″**, **hr′**, **hr**, **rh^W**, **rh^X**, **rh^{W_2}**, and **hr^V** (*cf.* Table 2).

Table 2: Comparison of Wiener's and Fisher-Race's Interpretation of Rh–Hr Serology and Genetics

	Year	*Gene or 'Chromosome'*	*Agglutinogens*	*Blood Factors Present*
Wiener	1945	R^1	Rh_1	**Rh_0** and **rh′**
	1960	R^1	Rh_1	**Rh_0**, **Rh^A**, **Rh^B**, **Rh^C**, **Rh^D**, **rh′**, **rh_i**, **rh^G**, **hr″**, **hr^S**, and **Hr**
Fisher-Race	1945	CDe	C, D, and e	C, D, and e
	1960	CDe	C, D, and e	C, D, and e

Note. As can be seen, Fisher's synthesis of 6 (or 5) factors has as little to do with the 18 known blood factors as the 4 elements earth, air, fire and water, of the Ancients have to do with the elements of modern chemistry.

In 1944, Fisher,[24] a pure mathematician, apparently unaware of or disregarding Wiener's earlier work, again attempted to account for the heredity of Rh–Hr types by a theory of linkage, one of the possibilities previously disproved and discarded by Wiener. To the 4 blood factors known at that time, **Rh_0**, **rh′**, **rh″** and **hr′**, he assigned the letters D, C, E, and c, respectively, and predicted that d and e would be found. According to him, there were 3 pairs of allelic genes, D–d, C–c and E–e, which are inherited in linked sets of 3 genes each (*triple inheritance*), each gene determining its corresponding agglutinogen. In this simplified hypothesis, each agglutinogen was considered to have a single corresponding antibody, and since the distinction between agglutinogens and their serological attributes could therefore be disregarded, the terms *agglutinogen* and *blood factor* were used interchangeably. This was hailed by Race and Sanger as Fisher's so-called 'synthesis' and the claimed fulfillment of his 'predictions' was considered proof of the validity of the hypothesis, and justification for the adoption of the C–D–E symbols in place of Wiener's Rh–Hr terminology.

The nature of this so-called 'proof' of Fisher's synthesis can best be shown by quoting from the books of Race and Sanger,[25] Kabat,[26] and Roberts.[27]

Race, R. R. and Sanger, R. (1958): *Blood Groups in Man*, 3rd ed., p. 123:

'The finding of the remaining antibody, anti-d, was first reported by Diamond in 1946. Two further examples were reported by Hill and Haberman in 1948. The specificity of these antisera are now in considerable doubt . . . Such successful [*sic*] predictions must be rare in biology . . . Violent attacks on the theory, in the publications and correspondence of Dr. Wiener, must run into many hundreds'.

Ibid., p. 162:

'The discovery of anti-f has called into question the reported examples of anti-d and it now seems very unlikely that this antibody has ever been found'.

Kabat, E. A. (1955): *Blood Group Substances*, p. 13:

'Fisher postulated that two additional factors d and e existed, and that anti-e and anti-d would be discovered which would make these two antigens detectable. Subsequent studies have fully [*sic*] confirmed this prediction. Anti-e was discovered by Mourant . . . Anti-d was reported by Diamond and subsequently by Hill and Haberman *et al.*; it occurs extremely infrequently . . . so that Wiener has expressed doubt of its existence. More recently Rosenfield *et al.* have recognized a new Rh factor, f . . . It is now generally thought that the anti-d was probably anti-f.'

Roberts, Fulton (1960): *An Introduction to Human Blood Groups*, pp. 34–35:

'Fisher's predictions were confirmed and the two antibodies having the reactions expected of them, were apparently [*sic*] discovered . . . The reader may feel that he has been the victim of a deceit [*sic*] in that the whole argument has been built on the existence of d and the nature of its difference from D . . . The presumption of d's existence is a matter of convenience in exposition and will be maintained, but it is necessary always to bear in mind that the existence of d is not proved.'

Thus, these writers first cite the discovery of anti-d as confirmation of Fisher's synthesis; then, after it has served their purpose, they confess that the supposed discovery of anti-d is nothing but a myth. One must be an accomplished paradoxer indeed to be so proficient in double-talk! Apparently some readers are so uncritical that they fail to recognize the 'deception' and, as a result, another blood grouping myth bids fair to become a permanent part of the literature of the blood groups. The simple CDE/cde 'synthesis' created from thin air by a mathematical metaphysician continues to be taught (*cf.* Table 2), while the observations of pioneering, experienced serologists and the recommendation of the Committee on Medicolegal Problems[28-30] that Wiener's Rh–Hr nomenclature be used exclusively, and C–D–E be discarded, are ignored. Instead, the mythical 'discovery' of little d continues to be used as 'proof' of the validity of Fisher's predictions and 'synthesis'. Since contradictions and fallacies never disconcert a paradoxer,[31] there is hardly any doubt that this tommyrot will continue to be taught behind the C–D–E iron curtain for a long time to come, to the detriment of the quality of the research being done there.[32]

Discussion

One may feel that this paper of blood group mythology is only of academic interest, and not the concern of the medicolegal experts. Why not therefore use the C–D–E notations instead of the Rh-Hr nomenclature, if one finds the former easier to 'understand' and teach? In this connexion, a story recently cited by Dr. M. Shapiro is pertinent, of the Irishman who agreed to accept Esperanto as the international language, but only provided that it was spoken in Gaelic.

Since the true expert prefers accuracy to simplicity, it has been maintained that the correct use of Rh–Hr nomenclature may be employed as one

of the criteria by which to judge the qualifications of an expert. The following example will suffice to demonstrate how faith in Fisher's C–D–E synthesis can give and has given rise to erroneous exclusions of parentage in medicolegal cases.

According to Fisher's 'synthesis' the factor E (**rh″**) has but a single reciprocally related factor e (**hr″**), so that parents EE cannot have ee children, and ee parents cannot have EE children. Wiener's theory is non-committal on this point since, as has been pointed out, the specificity of new antisera still to be found is largely unpredictable. Now, in a magnificent paper of fundamental significance, Shapiro[33] finds that there are actually at least 2 blood factors **hr**^{S} and **hr″** reciprocally related to **rh″**. Anti-**hr**^{S} and anti-**hr″** are almost identical in specificity, since almost every blood that has factor **hr″** also has the blood factor **hr**^{S}, except among Bantu. Therefore, if the antiserum labelled anti-e is of specificity anti-**hr**^{S} instead of anti-**hr″**, false exclusions of parentage can result, especially in medicolegal cases involving negroes. In fact, there is evidence[34] that such errors may have been not infrequent in the past. The earlier work of Wiener and Unger on the blood factors **Rh**^{A}, **Rh**^{B}, **Rh**^{C} and **Rh**^{D} associated with blood factor **Rh**$_0$ is, of course, in the same category as Shapiro's recent report on **hr**^{S}.

As for the medicolegal implications of the claims of associations between particular A–B–O groups and disease, reference may be made to Graubard's[35] assertion that all patients with Dupuytren's contracture tested by him belonged to type Rh_1Rh_2. This fantastic report has been quoted in the courtroom by medicolegal experts as evidence that Dupuytren's contracture is a constitutional disease, when testifying on behalf of insurance companies defending claims for compensation on the grounds that the disability is occupational in origin.

The present plight of the blood grouping field may be ascribed to the intrusion of mathematicians into the subject, and the substitution of complex calculations for laboratory observations and common sense. Thus, instead of permitting the serological results to speak for themselves, papers are published with an impressive facade of chi square computations, and the maximum likelihood method is applied to calculate gene frequencies to the eighth significant figure,[36] based on a few scores of incorrect tests carried out by biometricians, anthropologists and others untrained in serology. It is time to discard such computations and to restore the laboratory to its rightful place in serology.[37] Then, workers will again be compelled to use their brains for thinking instead of operating calculating machines. Blood group mythology may suffer, but the field of blood grouping will regain its position as a respectable science.

Summary

Most of the 'pitfalls' in medicolegal serology are due to inadequate training and lack of understanding. Unfortunately, most of the available texts are

replete with misinformation, and written in such a misleading fashion as to leave the reader with many serious misconceptions.

The purpose of this article has been to expose this modern blood group mythology so as to place the neophyte on his guard, and to direct him to reliable sources of information, in order that his mind may not be poisoned with wrong ideas that will impair his future usefulness as a medicolegal expert.

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British Association in Forensic Medicine

Meeting held in Oxford, 26–27 June 1959

Symposium: *Therapeutic Misadventures*

Speakers

Morning Session: Dr. F. E. Camps (*President*), opening remarks.
Prof. H. Gormsen (*Copenhagen*).
Prof. C. Simonin (*Strasbourg*).
Prof. W. Laves (*Munich*).
Prof. L. Roche (*Lyon*).
Prof. Derobert (*Paris*).

Afternoon Session: Dr. T. K. Owen (*Bournemouth*).
Dr. Milford Ward (*Leicester*).
Dr. H. Johnson (*London*).
Dr. C. Corby (*London*).

Opening Remarks by Dr. Camps

Gentlemen: First of all I would like to apologise for the absence of Dr. Teare. I would like to welcome on your behalf representatives of several other countries and say how pleased we are to see them here to-day. We have Professor Roche from Lyon, and although Professor Derobert of Paris cannot be with us he has sent his paper for us to read. Other new visitors are Dr. Obersteg from Basle, Professor Simonin from Strasbourg and our old friends, Dr. Thomas and Dr. Van Hecke, from Belgium, Professor Laves from Munich and Professor Harald Gormsen from Copenhagen. I would also welcome two other distinguished visitors from England, Air Comm. Stamm and Mr. J. P. Reidy, Plastic Surgeon at Stoke Mandeville hospital; from Professor Kerr's department in Edinburgh we have Dr. Ranasingh.

The subject for discussion to-day was chosen because a similar discussion was held in Paris last year; and I only wish that our organization was as good as theirs. Their speakers were literally queueing up in the doorway to carry on where the one before had left off. They were so good and interesting it seemed that we had a nucleus to take from there.

The type of therapeutic accident we have aimed to discuss to-day is not the type of accident where malpractice is concerned. It is a problem of distinguishing between negligence and a preventable accident.

I understand that Mr. Reidy has brought some very interesting slides to show us and I believe Dr. Thomas will read the paper sent over by Professor Derobert.

One of the difficulties in a small Society of this sort is to have simultaneous translation. Some papers will therefore be read in French and I have arranged for someone to do a short translation afterwards for those who cannot follow them.

Without further ado I will call upon Professor Gormsen who should rightly take the first place in this programme, to talk about *Therapeutic Misadventures in the Last Few Years in Denmark.*

On Therapeutic Misadventures in the Last Few Years in Denmark

Harold Gormsen, M.D.

University Institute of Forensic Medicine, Copenhagen

According to Danish law, on death registration *every* case of accidental death *must* be reported to the police. (We have no Coroner system). Every case of lethal therapeutic misadventure reported to the police will, before a possible trial, be submitted by the police to the Medico-Legal Council (a state advisory board of medical experts appointed by the Ministry of Justice) for an expert opinion as to whether negligence has taken place or not.

It should thus be easy to sum up the figures and the categories of therapeutic misadventures in our country by going through the files of the Medico-Legal Council.

However, not all lethal therapeutic misadventures are reported to the police. Operation accidents and anaesthetic deaths in hospitals will be frequently not reported. Ordinary death certificates of heart failure will often be issued in these cases.

Thus the figures that I am going to present must be taken *cum grano salis* as far as hospitals are concerned; whereas I feel sure that you can rely on the figures concerning practitioners and practising specialists, since I have confined this paper to include lethal therapeutic misadventures only. Lethal cases due to diagnostic mistakes and sins of omission are left out of this review.

The death cases due to therapeutic and diagnostic misadventure submitted to the Medico-Legal Council during 1944-1956 are presented in Table 1.

TABLE 1: Deaths due to Therapeutic and Diagnostic Misadventures Reported during 1944-1956 to the Danish Medico-Legal Council

1. Erroneous medication (mistakes, overdosage)	20
2. Anaesthesia	15
3. Various therapeutic procedures	10
4. Anaphylaxis	9
5. Various diagnostic procedures	6
Total	60

There are about *5 cases a year*, i.e. there is about
One case a year per 1000 physicians; or
One case a year per 1 million inhabitants.

Hospital: 32 cases.
Practitioners and Specialists: 28 cases.

Comments on Group No. 1:

Among the 20 cases of erroneous medication there were:

4 cases after administration of *morphine/scopolamine/barbiturate* in *ordinary* doses to cases of alcohol intoxication;

3 cases after administration of *morphine* in *ordinary* doses to persons under the influence of *barbiturates* (*synergism of drugs*).

Comments on Group No. 2:

The 15 anaesthesia cases comprised:

Ether	5	(1 case of aspiration of vomit).
Ethyl chloride	2	
Chloroform	2	
Evipan (Intravenous)	1	
Faults in apparatus	2	
Spinal anaesthesia	1	
Local anaesthesia	2	(1 overdosage of Percain). (1 overdosage of Adrenaline).

Total: 15.

Hospital: 10; *Practitioners:* 3; *Practising Specialists:* 2.

Comments on Group No. 3:

The 10 cases of various therapeutic procedures comprised:

Slipped ligatures	2	
Air embolism	2	(One of insufflation in the Eustachian and one of the Fallopian tubes).
Electric shock	3	
Transfusion	1	(ABO incompatible blood).
Oxygen catheter in the oesophagus	1	(stomach rupture).
Swabbing of pharynx	1	(pharynx lesion with retro-pharyngeal haematoma).

Total: 10.

Comments on Group No. 4:

The 9 cases of anaphylaxis comprised:

Salvarsan	4
Penicillin	2
Tetanus-antitoxin	2
Desensitization for asthma	1

Total: 9

Comments on Group No. 5:

The 6 Cases of various diagnostic procedures comprised:

Bronchoscopy	2	(mediastinitis via a lesion of the larynx and oesophagus, respectively).
Oesophagoscopy	1	(mediastinitis).
Sternal puncture	1	(haemopericardium).
Suboccipital puncture	1	(subarachnoid haemorrhage).
Carotid-arteriography	1	(thrombosis).

Total: 6.

As regards the legal proceedings in these 60 cases, the charge was withdrawn in 53 cases because the Medico-Legal Council characterized the cases as accidental.

Legal proceedings were taken in the remaining 7 cases with the following results:

Two doctors, two nurses and one pharmacist were convicted of negligent homicide and fined; two doctors and two nurses were fined for offences against the Medical Act and the Trained Nurse Act, respectively (the section on gross negligence).

These cases will be mentioned briefly:

1. *An anaesthetist* who was responsible for the blood transfusions in the ward, but who was personally engaged in the difficult narcosis of the patient concerned, was convicted of negligent homicide in the transfusion case for having omitted to compare the patient's blood group card with the blood group stated on the bottle (a wrong bottle had been delivered from the Blood Bank), whereas the nurse who had supplied the wrong bottle in the Blood Bank was acquitted of the charge.

2. *A doctor and a nurse* were convicted of negligent homicide, because the nurse, owing to a misinterpretation of the written instructions of the ward, accidentally gave a 2-year-old child a tenfold overdose of barbiturate (Phenemal) as premedication for urography. The nurse consulted the doctor twice regarding the dose, while the latter was drawing a blood sample from a screaming child. The first time the doctor referred her to the instruction book and when, the second time, she said that the dose was stated as 160 centigrammes in the instruction book, the doctor said—without reflecting further on the question—that 'if the instructions said so, it had presumably to be right'.

These two cases show how dangerous it may be to do more than one thing at the same time.

3. *A doctor* telephoned a prescription for a tannin solution for use as an enema. The pharmacist thought he heard it as a strychnine solution and dispensed the latter in the concentration prescribed. The doctor was acquitted, but the pharmacist was convicted of negligent homicide, because the dose prescribed exceeded the maximal dose of the Pharmacopoeia.

4. *A nurse* was found guilty of negligent homicide because by mistake she had given a patient *phenol* as an enema instead of something harmless.

5. An otologist injected for tonsillectomy a Percain-Adrenaline solution which the nurse had prepared. Unfortunately, the nurse had prepared a solution for surface anaesthesia, so that the patient received by injection 15 mg. of adrenaline and died promptly.

The doctor and the nurse were sentenced for breach of the Medical Act and the Trained Nurse Act, respectively, the doctor for gross negligence, because he had not made sure that the nurse poured out of the right bottles. It was said in the judgment: 'A doctor who gives a patient an injection has the sole responsibility for the injection made . . . and it is the doctor's indispensable duty . . . to the greatest possible extent, to make sure that the liquid he injects is the right one, among other things by looking at the label of the bottle'.

In the last two cases a doctor and a nurse were sentenced for breach of the Medical Act and the Trained Nurse Act, respectively, for prescribing too large doses of barbiturates to a patient, and for injecting, by mistake, too large a dose of morphine.

In only one of the 60 cases a doctor was sentenced to indemnify the dependants for the loss of their bread-winner (£1,500, overdosage of Percain in local anaesthesia).

For the last $2\frac{1}{2}$ years I have no survey but I will mention a few cases.

I regret to say that we have seen several cases of fatal synergism, both of morphine-scopolamine and of barbiturates given to persons under the influence of alcohol, and particularly of morphine to persons under the influence of barbiturates, despite the fact that several articles with warnings have been published on this subject in the last few years.

In 1958 the most serious catastrophe due to therapeutic misadventure in the history of medicine in Denmark took place in Copenhagen. In the course of a few days 9 patients died and a number of patients had more or less severe reactions following *transfusions of blood* from a hospital blood bank. The ensuing investigation showed that most of the blood units stored in the bank were heavily contaminated with Gram-negative bacteria, *Pseudomonas fluorescens*. At the autopsies signs of severe shock were found in all cases, including suprarenal haemorrhages, and in several cases Pseudomonas of the same strain as that in the bottles was cultured from the blood and the organs.

It was further found that the contamination of the blood was *not* due to faulty sterilization of equipment, but had occurred in connection with the donor bleeding. In order to facilitate the insertion of the cannula of the bleeding set into the rubber diaphragm of the bottle, the phlebotomists moistened the rubber with an antiseptic solution containing phenyl mercury acetate. However, it was later shown that this antiseptic was unsuitable for this purpose and that gross contamination of the contents of the bottles was possible using this technique.

There was no legal prosecution in this case. In the view of the Medico-Legal Council and the Prosecutor nobody could be held responsible for not realizing the danger of the technique used.

Further I should like to mention some cases of so-called *soap embolism*. We have about 5,000 cases of therapeutic abortions per year in Denmark and for a number of years several hospitals have been using as a therapeutic abortion procedure, instillation in the uterine cavity of 35 ml. of a sterilized soap cream (Cremor Saponis Sterilisatum, with a pH of about 9.9 containing 20% fatty acids, i.e. about 22% soap). In the last few years 4 deaths have occurred in connection with this soap instillation. In 3 of the cases death occurred in collapse within a few minutes after the instillation; in the fourth case death occurred suddenly without any warning symptoms

about 16 hours after the procedure. The gross autopsy findings in these cases were negative, but histological examination of Sudan-stained frozen sections revealed intra- and perivascular Sudan-positive precipitates in the myometrium, parametria, lungs, kidneys and brain. Identical findings have recently been described by Schwerd (*Deutsche Zeitschrift für die Gesamte Gerichtliche Medizin,* **48,** 202, 1959) in deaths due to illegal abortions with soapy water.

There is hardly any doubt that the deaths were actually due to soap in the blood stream and the procedure has now been abandoned by several hospital wards.

Finally, I want to mention a recent case because it is so extremely unusual. A 31-year-old healthy blood donor complained a week after the bleeding of pain in the arm from which the blood had been drawn. The doctor found a superficial thrombophlebitis in the arm. During the following period he complained of dyspnoea and consulted the doctor 27 days after the bleeding. X-ray of the lungs revealed nothing abnormal. Thirty days after the bleeding he suddenly died.

Autopsy showed that a very thin cannula stilette 4 cm. long had perforated the posterior wall of the right ventrical of the heart; 1.5 cm. of the stilette projected on the posterior wall of the heart, and the pericardium contained 20 ml. blood. The hospital doctor who had performed the bleeding a month before explained that the cannula blocked when he had bled the donor of 250 ml. of blood. Therefore he re-punctured the same brachial vein, but could not remember whether he employed the same cannula or another one.

The stilette had probably been hidden in the cannula first employed and had inexplicably (presumably because the doctor had pressed the tube when the blood stopped running) been introducted into the brachial vein and later on been conveyed to the heart. The matter was settled out of court, the widow receiving compensation from the blood donor corps.

From a prophylactic pedagogic point of view it is extremely important that every case of death due to therapeutic misadventure be examined thoroughly. These cases ought to be published in the international periodicals more frequently than has so far been the case.

Double Fatal Poisoning after the Therapeutic Ingestion of Leaves of Colchicum Automnale on the Prescription of 'A Curer'

Prof. C. Simonin
Strasbourg

Poisoning by *Colchicum automnale* (meadow-saffron) is not uncommon in France. This medicinal plant is well known for its curative qualities; it is recommended by popular medical books and everyone can get it easily, since it grows in our fields.

Poisoning due to colchicum can result in litigation involving expert forensic opinion. Together with my toxicological colleagues, Duquenois, Jaeger and Weil, we were entrusted with a legal case which presented itself in the following circumstances.

A husband and his wife, aged respectively 74 and 68 years, died on the same day, in April, after violent colic, vomiting and diarrhoea. The doctor called in for the patients could do nothing but attend the last moments of Mrs. I; but he sent her husband to hospital where he soon died. In both cases, the death certificate stated: Natural death.

Twenty-five days later a charge was formulated before a tribunal. It accused a 'curer' named E, whom the couple consulted because they were suffering from rheumatism. The curer ordered plants which they were to ingest without any other preparation than cooking. As evidence to strengthen the charge the police took a sample of the plants from the couple's house.

The necropsy of the woman, which was made at the Institute of Pathology, showed the following changes:

Lungs—dark red, heavy and large weighing 620 to 720 g., and presenting an intense and diffuse oedema and hyperaemia with blackish-red small belts, looking like splenopneumonia.

There was no damage to the gastric mucous membrane; the intestinal contents were fluid with a little clot;

Spleen, 180 g.; Liver, 1,380 g.; Kidneys, thin cortex, light beige in colour, pale pyramids, well marked;

Nothing was noticed elsewhere.

The pathological diagnosis was intense oedema and hyperaemia of the lungs with the early stages of a splenopneumonia of the bases, complicated by a degenerative hepatitis and by a terminal epithelial nephritis.

The necropsy of the man took place only after exhumation, 25 days after his death. The relatively good preservation of the viscera permitted useful observations, which can be summarised as follows:

Hyperaemia of the gastric mucosa. The stomach contained a sticky meal with clear vegetable particles, which were removed for examination;

The lungs of a dark-red colour, deeply congested, weighed 500 to 700 g. and showed an apoplectical hyperaemia of the parenchyma of which certain portions sank in water. The heart was thick, soft, flaccid, red, and weighed 600 g.; greenish liver of 900 g.; intestines congested in places, containing some excrement and vegetable particles; blood in the urine; the kidneys weighed 150 and 100 g. respectively and were of a dark colour.

The cause of death could not be established with certainty. Nevertheless the hyperaemia of the gastric mucosa and of certain parts of the intestinal mucosa, the presence of bloody urine in the bladder and the apoplectical hyperaemia of the lung parenchyma suggested the diagnosis of acute poisoning.

In the case of the woman the same possibilities arose from the pathological observations in that the state of the kidneys and of the liver suggested damage of toxic origin.

The sum up, the facts observed at the necropsy and the clinical indications make suspect in both cases a death due to acute intoxication. It was then for the toxicologist to bring out the proof of the poisoning. There were no difficulties in identifying the plants which were seized at the couple's home. These plants had long leaves 15 cm. long by 1 cm. wide and had a system of two bulbs, surrounded by a dry brown membrane. Its organoleptical, anatomical and microchemical composition would correspond to *Colchicum automnale*.

In the stomach contents of the man, scraps of green leaves were found, of which the botanical characters corresponded to those of the leaf of *Colchicum automnale*.

The toxicological investigations were made on 100 g. of the stomach contents and confirmed the presence of *Colchicum automnale*.

The renal extract contained also an alkaloidal substance. One knows that about 50 g. of leaves of colchicum are enough to occasion the death of an adult. Subsequently in the stomach contents of the man about 250 g. of these leaves were found. This explains the speedy death of the man in less than 12 hours.

It was therefore established that the couple ingested a lethal dose of leaves of *Colchicum automnale*. The curer was condemned by the tribunal for a double involuntary homicide and for the illegal practice of Medicine. In our country, poisoning by this means is the consequence of the mistake which results from the confusion between wild garlic (*Allium ursini*) and meadow-saffron (*Colchicum automnale*).

The poisoning is observed in spring during the growth of colchicum leaves. Only the seeds of this plant are used in the preparation of colchicine, a very toxic alkaloid, from which therapeutic accidents are well known.

Therapeutic Misadventures

Prof. W. Laves
Munich University

Mishaps following injections or transfusion are seldom observed in general medical practice. In the course of the last few years we have had the impression that fatalities occur more often in hospitals or in clinics in the course of surgical operations. This may be due to the development of modern surgical methods, of the progress in anaesthetics and in the techniques of transfusion. One consequence of the present state of affairs is the need for more personnel, more surgeons, more nurses. The operating teams have not only been increased but the functions of the assistant doctors and the nurses have become more specialized, more self-responsible than they were before the era of artificial hypothermia, hypotension, etc. This situation gives rise to a number of occasions which may lead eventually to tragic accidents.

After a fatality the question of responsibility has to be examined. Which member of the team committed the decisive error? In some cases the investigation can be very difficult. The methods of Forensic Pathology do not always suffice to clear up the case; if for instance the primary injury has not caused characteristic pathological findings or if long continued attempts at resuscitation have influenced or changed the picture of the organic changes. Therefore it is in most cases necessary to obtain as many clinical observations on the development of the symptoms as possible and to compare the data with the post-mortem findings. Of a great number of observations, some unusual events will be briefly reported.

1. The So-called Zephyrane Case

A lady of 51 years intended to get married again, but before going to the church she decided to undergo a plastic operation to her face. The surgeon started with local anaesthesia on the right side, using Novocain-Suprarenin. The tightening of the skin was performed without difficulty. About 30 seconds after having infiltrated the subcutaneous tissue of the left cheek and of the left side of the neck, the skin became swollen and dark red. Paraesthesia of the left hand occurred. Respiration became irregular and dyspnoea set in. The surgeon performed an incision parallel to the insertion of the left ear. The subcutaneous tissue had a dark brown colour, the veins were thick and thrombosed, the left facialis nerve was paralysed.

The operation was interrupted and the wound closed superficially by some sutures. A check of the solution used for the anaesthesia revealed that about 20 ml. of concentrated Zephyrane had been used for the infiltration. The surgeon had the habit of cleaning the skin, using the concentrated solution of this disinfectant. He had ordered the assistant nurse to pour a considerable quantity of it into a cup, which was placed on the instrument table, together with a similar cup filled with the Novocain solution.

Immediately after the operation a pharmacologist was consulted. His opinion was that the symptoms would pass without dangerous consequences. During the next 24 hours the facial oedema intensified. Several incisions were made. Later a severe *anaemia* became apparent; the paralysis of the facialis nerve did not improve. The haemoglobin was found to have dropped to 32% and the number of red blood cells to 1,800,000 per c. mm. The white cells increased. In the following days vomiting occurred, blood transfusions were given but the urine secretion diminished, oedema of the hands and legs appeared, followed by symptoms of myocardial infarction and uraemia. The patient survived 14 days.

The post-mortem examination revealed dense infiltration of the left cheek and the side of the neck, combined with thrombosed veins, multiple myocardial infarctions in both ventricles, subendocardial ecchymoses, hydrothorax, degeneration and necrosis of the liver, nephrosis and oedema.

(Slides were shown demonstrating the appearance of the patient, photomicrographs of the pathological findings and spectrophotometrical absorption curves of the haematin : globin formation following addition of Zephyrane to blood (haemoglobin) solutions).

The surgeon was found guilty as well as the nurse who had exchanged the liquid by mistake.

2. Sudden Death Following an Intravenous Benzene Injection

In the waiting room of the operating theatre of a clinic, bandaging material together with a bottle containing Benzene had to be prepared for an outpatient. In the meantime a 23-year-old woman was admitted to the hospital with a provisional diagnosis of acute appendicitis. She was prepared for operation. The anaesthetist took a bottle labelled Pentothal-Sodium from his table, filled the syringe and injected intravenously very slowly about 8 ml. of the liquid. Suddenly intense cyanosis occurred followed by respiratory standstill. A Sister checked the liquid still present in the syringe and stated that it was probably Benzene. A thoracotomy was performed. Neither heart massage nor electrical stimulation had any resuscitating result. The patient was dead.

The post-mortem findings were reddish imbibition of the intima aortae, subendocardial ecchymoses, haemolysis, oedema of the lungs, no signs of an

appendicitis, and hyperaemia of the brain, liver and kidneys. The solution of this tragic misadventure was that the employee who had prepared the bandaging material had taken the empty bottle with the label Pentothal-Sodium out of a box removing the label and, after filling the bottle with Benzene, he had left the room. A short time later, a Sister had entered this room and, observing the bottle, had put it on the anaesthetist's table in the belief it was Pentothal-Sodium.

(Slides were demonstrated showing the influence of Benzene injections on the blood pressure of rabbits).

The finding of the court was that the nurse responsible for the operating room had stored empty bottles of Sodium-Pentothal without removing the labels. She was found guilty.

3. Air Embolism on the Occasion of a Plasma Transfusion

A patient 42 years old was admitted to hospital on account of an appendicitis. A laparotomy was performed but the appendix did not show any inflammation. A perforated gastric ulcer was found combined with bleeding into the abdominal cavity. During the examination the pulse became very weak. A plasma transfusion was started, using air pressure on account of an insufficient flow of the plasma. Unfortunately the assistant doctor who had to observe the level of the liquid during the transfusion, was called away for some minutes. Suddenly cardiac arrest occurred, the origin of which was at first unknown. After thoracotomy the heart appeared to be very voluminous. On massaging the heart in the usual manner a subcutaneous emphysema of the neck became evident. The surgeon decided to perform a puncture of the right ventricle. Blood mixed with abundant gas bubbles burst out. Further resuscitation failed.

Discussion: The air pumped into the bottle had been allowed to enter the veins during the absence of the assistant surgeon, i.e. through negligence.

4. Sudden Death Following 'Movellan' Injection

A boy 6 years old, suffering from enuresis, had been treated by intramuscular injections of 'Movellan', a preparation containing 10 mg. of Sodium-Strychnate. The treatment led to a recovery which lasted one year. After a relapse had occurred the mother took the boy on a bicycle to the doctor's office. The boy was injected intramuscularly with the same dose of 'Movellan' as before. After he returned home, cramps and convulsions began and the boy died showing symptoms of an acute strychnine poisoning.

The analysis of this case was very difficult because no overdosage had occurred. Finally the mother was questioned again. She told us that the boy, on leaving the doctor's home, had refused to take his seat on her

bicycle. He preferred to run after his mother and this took about 10 minutes. Shortly after arriving at home the convulsions started.

Discussion: Muscular exercise increases the blood flow through the muscles up to 10 times and more of the normal value. It was very probable that this had led to an accelerated absorption of the injected strychnine, which entered the blood stream in a toxic concentration.

5. Sudden Death following Strophanthin Injections (3 Cases)

This short report deals finally with 3 fatalities observed in 3 female patients of 42, 72 and 79 years. The women were suffering from cardiac insufficiency of some years' standing. They had been treated with 'Combetin' injections. The active principle of Combetin is *Strophantin combe,* in a dose of 0.125 mg. The injections were prepared on the critical day, and were to be used at 9 o'clock. The treatment could not be performed before 12.30. Immediately after the 79-year-old lady had been injected, paraesthesia, then cyanosis and tetanic contractions of the arms and legs started. The dyspnoea intensified and 10 minutes later death occurred. The same symptoms became evident in the two other women following the injections. They also died within 10 minutes. Resuscitation failed in all 3 cases.

The post-mortem findings showed coronary arterial sclerosis combined with severe calcification of the arterial wall in two cases and a fresh myocardial infarction in one case.

Discussion: Intensive interrogation of the assistant surgeon proved finally that the Combetin injections had each been given in a minimum period of 20 seconds. Since it is well known that elderly patients suffering from cardiac insufficiency may react in a pathological way to rapid injection of Strophanthin, this time was too short.

A prosecution was ordered.

Therapeutic Accidents From Overdoses of Drugs

L. Roche and L. Cotte
Lyon

Recent therapeutic advances have brought in their train an increased number of mishaps. Among these, accidents from overdosage form a homogeneous and well known group.

Physiology and Pathology. The mechanism of action of most of the drugs in question is well known and the effects of overdosage can be reproduced in animal experiments. These cases fall into two groups:

Acute poisoning due to massive overdosage; and
Chronic poisoning due to repeated doses.

The latter group is made more complicated by the habituation of the body to the drug, e.g. the administration of 500-1000 mg. of Chlorpromazine to a schizophrenic over the course of several weeks may bring on such effects as Parkinsonism so gradually that they only become apparent when the drug is stopped. The effects of overdosage must be distinguished from those of idiosyncrasy. The latter may occur even with prudent treatment and the symptoms are much more variable and unpredictable. In practice the distinction between overdosage and idiosyncrasy cannot always be sharply drawn, e.g. a normal dosage of digitalis reduced the pulse rate to 40 per minute and caused coupled beats in a woman of 80 years.

Prescriptions. The doctor has the legal right to prescribe any drug in any dosage he thinks fit, but when he wishes to exceed the maximum dose laid down in the Codex, he is obliged by law to endorse his prescription with the words ' I mean this dose ', and to write the dose in words. The pharmacist may only dispense doses above the official maximum if he has satisfied himself of the doctor's intention. In accidental overdosage due to errors in the prescription, the doctor and the pharmacist may both be liable.

The Aetiology of Acidental Overdosage. This is illustrated by the following personal observations.

1. *Prescription of Large Doses.* In stubborn cardiac arrhythmias the doctor may be obliged to use digitalis in high dosage. The same is true of the use of opiates in cancer patients. In such cases the risks have to be accepted.

2. *Errors in Administration.*

(*a*) *The Patient may exceed the prescribed dose*:

A man of 28 with a painful bladder stone was prescribed Palfium (pyrolamidol), 4 tablets daily. In a severe attack of pain he took 9 tablets

within an hour and went into deep sleep. The doctor called 4 hours later and found him dead. At autopsy, besides the stone, there was nothing except moderate pulmonary oedema (Lyon Medical, 1958, **2,** pp. 785-790).

(*b*) *Nurses' Errors*:

A man of 33 with mild diabetes while on a journey—had an injection from an orderly, who gave him the entire contents of the bottle—about 400 units of PZI. He survived, but needed 1,720 grammes of glucose in the next 4 days (Societe de Medecine Legale et Criminologie de France, Seance du 13 Oct., 1958).

(*c*) *Doctors and nurses' errors*:

Misprints in professional journals can have grave consequences. In such a case a journal was successfully prosecuted.

(*d*) *In children*: There have been two cases of overdosage with aluminium salicylate used to control diarrhoea. One of them was in a baby of 4 months who arrived at hospital with a respiratory rate of 70 per minute and a pulse rate of 160 per minute and died the same day; 7 tablets of Aluvozal had been given.

Another baby of 6 months had been given 10 tablets but survived after correction of a greatly reduced alkali reserve.

A baby of 3 months with diarrhoea and vomiting was given Largactil 9 min., cortisone 40 mg., and atropine 30 min. daily for 8 days together with antibiotics and subcutaneous saline. On admission intestinal obstruction was diagnosed with oedema and an enlarged heart with gallop rhythm. Death ensued in a few days.

3. *Criminal Poisoning.* Such cases are rare but the recent insulin murder is well known.

4. *Medico-Legal Responsibility in Cases of Overdosage.* In French law there are no special statutes covering medical negligence. Such cases come under the provisions of the civil code concerning negligence, or under the criminal law. The doctor, the pharmacist or the nurse may severally be responsible in law, but in some cases the responsibility may be shared. A doctor is responsible for the nurse employed by him if his supervision has been inadequate, but not for an independent nurse. In actual practice the blame in cases of overdosage is seldom the doctor's.

Sales promotion campaigns by drug manufacturers carry the risk that doctors may be induced to prescribe excessive amounts of drugs with which they are not familiar.

In conclusion it is pointed out that the doctor's liberty to prescribe what he thinks fit carries with it a moral duty of care towards the patient.

Poisoning By An Organic Tin Compound (Di-iodoethyl Tin or Stalinon)

Summary

Prof. L. Derobert
Paris

This product was put on the market in France some years ago under the name 'Stalinon with Vitamin F' and was recommended for the treatment of staphylococcal infections such as boils, carbuncles and breast abscesses, in place of the tin derivatives previously used in such cases.

In France there were 210 cases of poisoning, of which 98 were fatal. A detailed analysis of the clinical features may be summarized as follows:

The clinical picture was dominated by oedema of the brain and spinal cord. The earliest and most constant symptom was severe generalized headache, beginning a few days after starting the drug. In addition, photophobia, vertigo, retention of urine, vomiting and abdominal pain were frequent, the last sometimes simulating appendicitis so closely that operation was carried out. Other features were hypothermia, bradycardia, rapid loss of weight, convulsions, confusion and coma. The chief neurological signs were meningeal irritation, transient or permanent hemiparesis or paraparesis, cranial nerve lesions, and aphasia. The fundus was usually normal, as was the cerebrospinal fluid. The EEG showed diffuse changes only.

The prognosis was grave and the best index of the chance of recovery was the state of consciousness. All the patients who went into coma died, with only one exception. Among the survivors, 84 made a more or less complete recovery, often after an illness of many months; 24 patients were left with permanent sequelae such as paraplegia, root pain, ocular paralysis, blindness and functional disorders such as anorexia or poor memory.

In the fatal cases the terminal events were convulsions (8), coma (38), syncope (20), circulatory or respiratory failure (28).

Discussion by Prof. Roche. This series of accidents made a marked impression in France. It took 10 months before new laws could be brought out to deal with the matter. The mistake was made by a pharmacist who had the wrong salt of tin.

Afternoon Session

A Fatal Accident During Bronchography

Dr. T. K. Owen
Bournemouth

In January 1953, a man aged 58 was referred to my hospital with suspected carcinoma of the lung. Six weeks before he had had an attack of pneumonia, which had failed to clear up. There was a persistent opacity on X-ray in the region of the right middle lobe. The left vocal cord was immobile.

It was decided that a bronchogram should be done. On 23 January 1953, 18 c.c. of Dionosil in aqueous solution were introduced through a tube into the trachea. Forty-five minutes later in the X-ray department, he suddenly became intensely cyanosed and died a few minutes later.

Post-mortem examination revealed extremely voluminous, emphysematous lungs; the trachea and the main bronchi and first divisions were blocked by coagulated paste-like material. The right middle lobe or lingula showed consolidation and was adherent to the chest wall. No neoplasm was seen. The heart was slightly enlarged (weight 13 oz.) but there were no other noteworthy findings. The cause of death clearly was asphyxia due to the injected material.

Subsequently it was revealed that the Registrar who performed the examination, because aqueous Dionosil had not been giving very satisfactory X-ray pictures, had added approximately 2 c.c. of the oily Lipiodol. This was stated to have been done on the instructions of the Consultant, and had been done on several previous occasions. A simple experiment of mixing the 2 solutions in a Petri dish soon showed that they do not mix, and that there is a reversal of phase, resulting in the formation of firm, paste-like material.

Dionosil was introduced in 1952, replacing Lipiodol, as the latter lingered a long time, particularly in diseased tissues, and occasionally gave rise to oil granuloma. Dionosil had only recently come into use in the hospital and it was not appreciated that there must be no delay in taking the X-rays after introducing the material, because the shadows are very transient.

This unfortunate happening was part of the price of progress, and is not likely to happen again, as an oily solution of Dionosil has now been introduced. Microscopic examination of the diseased lung showed only organizing pneumonic exudate. There was no new growth.

At the Inquest the widow expressed her gratitude to the Registrar for the kind way he had always treated her husband and there was no legal action.

'Always Read The Label'

Dr. Milford Ward
Leicester

Mr. President, Gentlemen: I only offer this short paper at the urgent request of your Secretary; I offer it under the title *Always Read the Label, or Should You* and he, in his wisdom, has deleted the last 3 words. I crave your indulgence in re-inserting them into the title, the reason being that I have selected 2 mishaps that occurred very many years ago at different hospitals, but which appear to illustrate both the importance of reading the label and also making sure that the label applies to the contents of the container.

The first case occurred immediately after the last war. A patient was admitted for cystoscopy as a day case to a large general hospital. As was the practice, he was put at the end of a very long list and appeared in the theatre about 7 p.m., when the operating session had been in progress since 9 a.m. with only a break for coffee and lunch. The nursing staff were also somewhat depleted at that time owing to the nurses' evening meal.

The theatre to which he was taken was the right-hand of a pair of operating theatres, and it so happened that the nurse attached to the anaesthetist for this theatre had gone off duty, leaving the anaesthetist unattended. The patient required a spinal anaesthetic for this investigation. The spinal anaesthetics were kept in a cardboard container on the lower shelf of the anaesthetist's trolley. When the anaesthetist came to inject the anaesthetic, she looked round for a nurse to open the ampoule of Nupercaine, but no nurse was actually in the vicinity. After a delay of a few minutes, during which time the surgeon was proceeding with his washing-up, a nurse came out of the left-hand theatre, was called by the anaesthetist and asked to take an ampoule out of the box, open it and present it so that the anaesthetist could fill the syringe. This she did and, as was the usual custom, placed the used ampoule on the trolley. It unfortunately slipped off, fell on the floor and was broken.

The spinal anaesthetic did not go well. The patient appeared restless and complained of headache, the degree of anaesthesia was very poor; but the surgeon was able to complete his cystoscopy and the patient returned to the ward and was not seen again by the surgeon.

During the evening he was obviously not recovering in the ordinary way from a spinal anaesthetic, complained of severe headache, vomited and collapsed. The anaesthetist, being somewhat suspicious of what had

occurred, returned to the theatre to investigate the contents of the box which should have contained ampoules of 3 c.c. of Nupercaine. Amongst 5 or 6 ampoules of Nupercaine she found one of Vinesthene. How this Vinesthene was put into the carton of Nupercaine was never discovered. At that time, owing to war shortages, the Vinesthene was being issued in clear glass phials instead of amber glass. It was not issued with any colouring matter and therefore was indistinguishable from the colourless Nupercaine. The ampoule was etched, but the etching was not very easily seen. The nurse had not presented the ampoule for the anaesthetist to read the label before opening it; she said she was asked to take an ampoule out of the box and that is all she did. The anaesthetist said that the carton was labelled Nupercaine on the outside and she accepted that the contents of the carton would all be Nupercaine. The pharmacist reported that the Vinesthene was issued in cartons containing 12 ampoules and, as far as he knew, they were kept in the same carton until used.

The patient died during the night and at autopsy the following morning I found numerous haemorrhages within the substance of both frontal lobes and gross engorgement of the spinal theca and of the ependyma of the ventricles. I expressed the opinion that death was due to the irritant effect of the Vinesthene when it had decomposed.

Vinesthene is the trade name for divinyl ether—a very unstable substance which should be kept in amber bottles and has a reducing agent incorporated. The instructions are that the fluid should be discarded if not used within 48 hours of the ampoule being opened. I understand that it is oxidized to formalin which, as you all know, is a very strong irritant.

At the inquest the Coroner said that he was quite satisfied that Vinesthene was injected into the spinal theca in mistake for Nupercaine, and he was of the opinion that this was the cause of death. He could not understand how the ampoule of Vinesthene got into the carton labelled Nupercaine, that the evidence disclosed negligence that was not of such a gross or culpable degree as to merit a verdict of manslaughter and produced a verdict of death from misadventure. There was a subsequent civil action which was settled out of court.

My second incident antedated the former by over 10 years and I may have been guilty of telling this story before; if so, I apologize. It has considerable interest to me since, in the civil action which followed the incident, the late Sir Bernard Spilsbury gave evidence against the doctor concerned in the case before Mr. Justice Oliver. This caused quite a lot of very unfavourable comment in the area. This again occurred during a week-end, in another general hospital in a ward of 24 children who all had rheumatic fever.

The resident in charge of the ward was away for the week-end and he had asked a colleague to keep an eye on the ward for him. About 12

noon on Saturday this doctor went into the ward and said to Sister: 'Have you anything you wish me to see?' Sister said that she had administered liquorice powder to the children as a routine measure that morning and that 8 of the children had been sick. They were reasonably comfortable at the time but the doctor asked to see the liquorice powder and went into the ward and looked at the patients. He did not examine them. The tin was an old cocoa tin on the outside of which had been stuck a label saying *Pulv. Liqu.* He looked into the tin and there was a yellow powder and it smelled as he would expect liquorice powder to smell. He therefore asked Sister to let him know if she was at all worried and left the ward to carry on round the hospital.

Around 1.30 p.m. he received a telephone call to say that one of the children had collapsed. He hurried into the ward and found one child moribund and another child seriously ill. He immediately instituted resuscitation of these 2 children and ordered all the other children to have a stomach wash-out. The second of the 2 children recovered after a somewhat stormy afternoon. At the autopsy on the fatal one, the important findings were:

A very severe gastritis and oesophagitis, an incidental finding was a fairly severe rheumatic pancarditis, with commencing mitral stenosis.

We then analysed the contents of the tin and discovered that instead of being liquorice powder it consisted of a mixture of pyrethrum and borax which was used in the hospital as an insect powder. Subsequent inquiry showed that the ward had had considerable trouble with ants and a tin of ant-insect powder had been issued. During stock-taking someone had produced the tin unlabelled and Sister looked at it, saw the yellow powder, smelled it, thought it smelled like liquorice powder and instructed the tin to be so labelled.

It had, on some previous occasion, obviously contained liquorice powder, the smell of which had persisted in the tin.

In this case the Inquest again produced a similar verdict, but this time the civil action was fought and, as I said, Sir Bernard appeared for the plaintiff. In his evidence he said that children did not vomit after liquorice powder and that when a group of 8 children out of 24 had vomited when a substance alleged to be liquorice powder had been given, the Doctor should have immediately suspected poisoning and should have washed out all their stomachs. He said that he had never known a normal child to vomit after taking liquorice powder. He also expressed his opinion that the degree of rheumatic disease of the heart that I had described was not significant and that the child would have made a complete recovery from his heart condition.

Unfortunately for the defence, Sir Bernard Spilsbury only spent a short time in Leicester, just long enough to give evidence, whereafter he left,

because the defending Counsel put the local paediatrician in the witness box who said that in his experience of looking after children clinically he found that vomiting after liquorice powder was so common as to be considered normal and he would not have been surprised if 8 out of 24 children had vomited. No one asked Sir Bernard when he had last treated a child or when had he last administered liquorice powder to anyone; nor did anyone ask him at what stage in his career he had treated children with rheumatic fever.

The case was found in favour of the plaintiff, damages of £500 were awarded, distributed in the relation of £450 against the doctor and £50 against the ward Sister.

We all wondered what else this doctor could have done. He was only in temporary clinical control; he looked at the powder, he had smelled the powder; it looked like liquorice powder to him, it smelled like liquorice powder, it was labelled liquorice powder—how was he to know that it was not what it appeared to be. That is why, *Mr. President,* I felt it wise to call my paper by the title *Always Read the Label—or Should You.*

Therapeutic Accidents

Adrenaline Poisoning

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Deaths from accidental overdoses of adrenaline are probably not as uncommon as is generally believed. Three proven cases have been studied in the Department of Forensic Medicine during the last 8 years. All these were due to injection. In addition, one case was examined in which death was undoubtedly due to hyperadrenalinaemia associated with traumatic haemorrhage into a paraganglioma due to palpation before laparotomy for an abdominal tumour (the paraganglioma).

The causes of the accidental injections bear examination. In one case it was due to the surgeon who incorrectly wrote on the script when ordering a solution for local anaesthetic. In the second it was due to an injection of 1/1000 adrenaline from a gallipot of 1/1000 adrenaline similar to that used for solution for local infiltration when performing a Caldwell-Luc operation. In the third case, it was due to aspiration of 1/1000 adrenaline from a bottle believed to contain a local anaesthetic solution, both bottles having similar labels.

All such cases present great difficulty in establishing the cause of death from the autopsy or examination of material from the autopsy, because adrenaline rapidly decomposes and disappears from the tissues. Attempts made in one case to recover the drug from the tissues were unsuccessful.

In all cases, however, examination of the fluid used for injection gave the full explanation, but should this not have been saved, proof of the cause of death would have been impossible.

Case 1

A healthy woman of 36 years, by profession a ballroom dancer, attended hospital as an out-patient for a plastic operation on the left breast. She had previously had plastic operations on both breasts and on the day in question she came in for a minor 'tidying-up' procedure under local anaesthesia.

At 2.30 p.m. the surgeon infiltrated with 40 c.c. of a solution of local anaesthetic. The surgeon had herself prescribed the solution, which arrived in 2 bottles labelled 'A': Adrenaline sufficient to produce a 1/1000 solution when added to 'B'; and 'B': The solution Novocaine. Sufficient

to produce a 0.5% solution when added to 'A.' Contains chlorocresol 0.1% (Fig. 1). The contents of the two bottles were mixed in a jug and it was 40 c.c. of this solution which was injected.

Fig. 1:

About 10 minutes later the patient became distressed. She said she was going to be sick, was sick, retched but did not bring up much: her breathing became gasping after she had been sick and then ceased.

Autopsy showed her to be a fairly well nourished woman with moderate cyanosis. There was an old operation scar on the left breast and a recent operation incision, 4 inches long, on the right breast adjacent to an old scar. There were 5 needle puncture marks, 3 on the outer side of the incision and 2 just internal to the old scar. Both pupils were widely dilated. Internal examination showed congestion of the brain with slight flattening of the convolutions. There was some bruising of the left side of the larynx and on the posterior oesophageal wall. Both lungs showed some basal collapse without gross oedema. The bronchi were hyperaemic and contained some yellowish material. There were scanty subpleural haemorrhages. The right side of the heart was slightly dilated and the left ventricle contracted. The muscle was pale. The valves and coronary arteries were healthy. The aorta was small and hypoplastic. The stomach contained a moderate quantity of partially digested food; its mucosa was congested. Apart from some congestion of the liver and the kidneys, the other organs were healthy.

Analysis of the two solutions A and B confirmed that they did in fact contain 1 : 1000 adrenaline and 0.5% Novocaine respectively, whereas it should have been 1 : 50,000 adrenaline and 0.5% Novocaine.

Case 2

A healthy male medical student, aged 21 years, was admitted to hospital for a Caldwell-Luc operation. He had been suffering from headaches due to a chronic antral infection for 3 years.

On the day of operation, at 8.45 a.m., he was given Omnopon gr. 1/3 and scopolamine gr. 1/150, and at 9 a.m. his nose was packed with 2% cocaine and adrenaline gauze. At 10.10 a.m. he was given thiopentone 0.75 g., Flaxedil 80 mg. and 1 c.c. of 10% cocaine spray with oral intubation and passage of an endotracheal tube which was packed off with saline gauze. Through this nitrous oxide, oxygen and Trilene were given in the prone position.

At 10.20 a.m. the surgeon infiltrated the mucosa of the gum margin with 8 c.c. of adrenaline (made up as 10 minims in 1 fluid ounce of normal saline). Five minutes later the pulse rate and respirations became very rapid and then ceased about a minute later. At 10.25 a.m. the patient was put in a head down position and the heart restarted, only to stop again 5 minutes later. Coramine 5 c.c. was given and 5 c.c. of 1% Procaine intravenously at 10.35 a.m., with recovery of pulse and respirations. Five minutes later the heart and respiration failed again; 5 c.c. of coramine was given into the right auricle and cardiac massage started at 10.45 a.m. Throughout the whole period the lungs were inflated with oxygen. The patient was pronounced dead at 11 a.m.

After the operation the anaesthetist collected the gallipot from which it was said the adrenaline had been drawn into the syringe, together with the bottles of adrenaline and cocaine.

Autopsy at 5 p.m. the same day showed a well-nourished, powerfully-built man. The left nostril was lightly packed with cotton wool which was slightly blood stained. A left Caldwell-Luc had been carried out. The brain was congested. Both lungs showed moderate collapse and some chronic thickening of bronchi with dilatation. There was a well-marked residual thymus. The left ventricle was slightly thickened and there were haemorrhages on the pericardial surface. The valves were healthy. The aorta was hypoplastic and rather small with definite narrowing at the site of the ductus and small patches of atheroma adjacent to the coronary artery openings. The spleen was healthy: it weighed 215 g. The other organs were acutely congested.

Analysis of the fluid in the gallipot showed it to be adrenaline 1 : 1000 and not 1 : 50,000, although the bottle labelled 'Sterile normal saline

Liq. Adrenaline μx – 1 oz.' from which the contents of the gallipot were said to have been poured, did in fact contain adrenaline μx in normal saline 1 fluid ounce as stated on the label.

Case 3

A primipara of 29 years was admitted to hospital in labour at 7 p.m. A breech presentation was diagnosed. The patient had good contractions, one every 5 minutes, and the foetal heart rate was 130 per minute, regular and of good volume. At 8.15 p.m. the patient was fully dilated and at 9 p.m. a breech appeared at the vulva. The surgeon prepared to perform an episiotomy under local anaesthesia and took a syringe from a trolley which was already set up. He asked the night sister for 2% procaine. She took a small bottle from the trolley and the surgeon withdrew 6 c.c. which he infiltrated into the patient's perineum. Two or three minutes later the patient complained of severe headache, sore throat and suddenly grew pale. A general anaesthetic (atropine, Pentothal and gas and oxygen) was given in order to deliver the baby as soon as possible. A living child was delivered and the episiotomy sutured, but all efforts to resuscitate the patient proved unavailing. The bottle from which the 6 c.c. had been taken when re-examined was found to be labelled ' Adrenaline.'

Autopsy showed a well-nourished somewhat heavily built woman with breast changes and evidence of recent delivery with suture of the perineum, which showed some oedema on the right side. There was marked cyanosis of hypostasis, lips and extremities. The brain was congested with moderate oedema. The laryngeal mucosa and the trachea were slightly congested and the air passages contained a little oedema fluid. Both lungs were spongy with slight collapse and oedema. The heart muscle was flabby: there were no subendocardial haemorrhages. The valves were healthy. The aorta was hypoplastic with slight narrowing at the ductus ridge. The stomach was congested in the mid-zone. The spleen was enlarged, weight 11 oz. The kidneys were congested and slightly swollen. The right ovary contained a corpus luteum. The uterus was enlarged to a full-term pregnancy with a plum coloured lower segment. There was a large pedunculated fibroid at the fundus with degenerative changes and smaller fibroids on the right side.

Attempts to recover adrenaline from specimens of blood and perineal skin were unsuccessful.

Case 4

This case illustrates an unusual accident during operative procedure.

A man aged 45 years had complained of vague abdominal pain for some time. He was in the habit of walking to his work and back each day, a matter of 5 miles each way, without any apparent discomfort.

He was found to have a tumour in the left upper abdomen and was admitted to hospital for laparotomy. He was given a general anaesthetic and, when relaxation occurred, the surgeon palpated the tumour before commencing the operation. The patient developed a very rapid pulse and died within a short time.

Post-mortem examination showed a large paraganglioma, measuring 10×5 cm. not connected with the left suprarenal gland and about 5 cm. above it. The tumour was found to have a haemorrhage into its substance, presumably as the result of palpation. Pulmonary oedema was not marked.

It is reasonable to suppose that death need not have occurred had the nature of the tumour been appreciated and proper measures taken to anticipate the complication. Nevertheless, even under ideal conditions, deaths are encountered when surgical interference takes place.

Discussion

Adrenaline is a short-acting sympatheticomimetic drug. It is a white, slightly alkaline powder, melting point 212° C., slightly soluble in alcohol and in water, giving an unstable solution which darkens on exposure to air.

It acts on the cardiovascular system stimulating the myocardium, accelerating the heart rate and increasing cardiac output, with a short-lived rise in blood pressure. Blood vessels in skin and mucosae are constricted, whereas the coronary arteries and vessels in voluntary muscle are dilated. It may alter the cardiac rhythm. These effects are modified by normal physiological mechanism, disease and drugs. In addition, adrenaline relaxes the bronchial musculature, elevates the blood sugar and blood lactic acid levels while at the same time decreasing the glycogen content of liver and muscle, and elevates body temperature, in part by its vascoconstrictor effect. It relaxes the gut and bladder musculature and constricts sphincters. Muscle fatigue is abolished and ocular pressure increased. The central nervous system is stimulated, causing anxiety and restlessness.

Adrenaline is not absorbed from the gut and is given either by subcutaneous or intramuscular injection or as an oral spray. Its effects are short-lived and the drug is rapidly oxidized or conjugated in the tissues.

Adrenaline has 6 main uses:

i. To control haemorrhage, particularly in ear, nose and throat surgery, as a 1 : 100,000 to 1 : 2,000 solution on pledgets.

ii. In conjunction with local anaesthetic agents for its vasoconstrictor effect to prolong anaesthesia and limit haemorrhage. It is used as a 1 : 100,000 to 1 : 20,000 solution, usually 1 in 50,000 and it is stated (Goodman and Gilman, 1955) that the total amount of adrenaline injected should not exceed 1 mg.

iii. Adrenaline is used in bronchial asthma as a subcutaneous injection of 0.2 to 0.5 ml. of a 1 : 1,000 solution or as an oral spray—0.5 ml. of a 1 : 100 solution inhaled over 3 to 10 minutes.

iv. In allergic disorders such as serum sickness and angioneurotic oedema, a 1 : 1,000 solution is injected subcutaneously up to 0.5 ml.

v. Adrenaline may sometimes be used in heart block (0.3 to 0.6 ml of 1 : 1,000 solution subcutaneously; and

vi. To elevate the blood sugar in hypoglycaemic coma (up to 0.5 ml. of 1 : 1,000 solution subcutaneously).

Adrenaline is prepared in the form of the hydrochloride or tartrate as a 1 : 1000 solution, to be diluted as required. The official pharmacopoeial dose is 0.1 to 0.5 ml. This preparation is sold in bulk form in bottles and in ampoules containing 1.0 and 0.5 ml.

The toxic effects are fear, anxiety, tenseness and restlessness, tremor, weakness, dizziness, pallor, throbbing headache, respiratory difficulty and palpitation. The blood pressure rises sharply and cerebral haemorrhage may result. The heart beat becomes irregular and may lead to ventricular fibrillation and cardiac arrest. These effects are particularly dangerous in patients with coronary artery disease or thyrotoxicosis. Used in conjunction with chloroform or cyclopropane anaesthesia, adrenaline may well be lethal.

Noradrenaline

By way of completeness some comments on noradrenaline are included.

This drug is closely related chemically to adrenaline, having one methyl group less in the amino group. It is prepared as the bitartrate, a colourless crystalline salt, very soluble in water giving an unstable solution. This is marketed as 4 ml. ampoules containing 0.2% noradrenaline bitartrate for intravenous use after dilution. Noradrenaline is pharmacologically similar to adrenaline but less marked in its effects. It has no broncho-dilator action and it does not precipiptate cardiac arrhythmias. It is used chiefly as a slow intravenous infusion in shock.

The toxic effects of noradrenaline are anxiety, awareness of a slow throbbing heart beat, headache, hypertension, photophobia, stabbing retrosternal or retropharyngeal pain, pallor, sweating and vomiting. The toxic effect, however, which has attracted the most attention and been well documented is the necrosis and sloughing of tissue at the injection site.

Cases of adrenaline poisoning are rarely recorded in the literature. Freedman (1955) in the *Lancet* reviews a series of 12 fatal and 4 non-fatal cases, including one of his own. These cases are collected from the literature from 1920 to 1955. In addition, 5 other fatal cases have been reported in the last decade. The references to all these cases appear at the end of this paper.

The principal causes of accidental adrenaline overdosage are failure to read the label on the container, leading to the wrong drug or wrong concentration being administered to the patient; faulty prescribing leading to too strong solutions being used; or the mixing up of minims and millilitres; or the giving of the wrong preparation to a patient, e.g. the oral spray solution instead of 1 : 1000 adrenaline subcutaneously to an asthmatic.

All such accidents could be avoided. The following suggestions are offered to help reduce the number of these cases.

1. It cannot be too often or too strongly stressed to every doctor, nurse or medical student, that he *must* read the label on the container and make sure it is the correct drug in the correct strength before administering it to a patient. It is not enough to read the label on the box; wrong phials can easily find their way into the box.
2. The abolition of the prescription of adrenaline in minims. All doses should be stated in metric units (milligammes and millilitres).
3. The use of special containers for bulk solutions which are easily recognizable.
4. The use of special distinctive labels on all adrenaline containers which are in complete contrast to the labels on local anaesthetic solutions.
5. The possible use of inert colouring material in pure adrenaline preparations.
6. Having a supply of piperoxan (an adrenaline antagonistic) immediately available when adrenaline is being administered for immediate intravenous injection should untoward symptoms occur.
7. Extreme care in selection and education of patients who self-administer adrenaline for asthma, with particular reference to solutions intended to use as a spray.

Summary

Three fatal cases of acute adrenaline poisoning are described, together with a fourth death from haemorrhage into a paraganglioma following palpation prior to laparotomy.

The pharmacology, uses and toxic effects of adrenaline and noradrenaline are described.

The literature relating to adrenaline poisoning is reviewed. Suggestions are made to help reduce the number of such poisonings.

My thanks are due to Dr. F. E. Camps for his assistance with this paper and allowing me access to his case records, and to Mr. A. Hardy for the photograph.

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Discussion

In the subsequent discussion Dr. Gresham (*Cambridge*) mentioned unusual transfusion disasters from infected blood and arterial granulomata after multiple transfusions in infants.

Dr. Dorward (*Dundee*) mentioned air embolism following artificial pneumoperitoneum in a pregnant woman.

Dr. Winstanley (*London*) mentioned adrenaline poisoning resulting from an illegible or inaccurate prescription.

Dr. Manning referred to a spinal anaesthetic disaster resulting from the cleaning of syringes by a detergent; and

Dr. Brittain (*London*) discussed foot drop from an injection into the sciatic nerve.

Therapeutic Accidents

During the Administration of Barium Enemas

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Deaths associated with accidents during radiological procedures are rare considering the number of examinations carried out each year. Nevertheless, by drawing attention to those that do occur, emphasis can be laid on the fact that there is a risk. Personal communications from various radiologists give the impression that there are a number of such accidents which do not terminate fatally.

The following cases illustrate 3 types of such accidents:

1. The introduction of an abnormal substance into the normal channels.
2. The introduction of the contrast media outside the normal parts to be outlined by traumatic rupture.
3. The introduction of the contrast media through the wrong channels.

Briefly:

1. Wrong substance.
2. Wrong technique.
3. Wrong place.

Accidental poisoning by Barium Enema containing Photographic Developer, Metol and Hydroquinone

One day in the Radiological Department of a London hospital 4 routine examinations of cases with barium enemas were carried out. The radiologist prepared the liquid for injection by putting into the enema jar 1½ pints of concentrated barium emulsion. He then prepared a concentrated solution of tannic acid, taking the powder from a sandwich tin on the trolley in the X-ray room. This was where the tannic acid was normally kept, being replenished from time to time from the bulk store which was

kept in a brown paper packet in a cupboard. He used 13 measures which were dissolved in a pint of water. He then poured this liquid on to the barium in the jar and added 9 pints of tap water. This gives a strength of barium of 3 oz. of the concentrated emulsion to the pint and of tannic acid about 1½% weight for volume. He had been mildly surprised and a little pleased to see the tannic acid tin full because the week before they had run out and no new large packet had appeared. He assumed that the Superintendent Radiographer, who was off duty that day, had filled the tin from the dispensary pending a bulk issue.

The first patient was a frail old lady of 71 years with almost fixed hips and very deaf, who was being investigated for subacute intestinal obstruction. After the barium had reached the descending colon the catheter came out and the patient was a little incontinent. No more barium was run in and films were taken and the patient helped to the lavatory along the corridor.

The next patient was a heavily built man of 64 years being investigated for right-sided abdominal pain. The routine filling of the colon was performed and he was finally sent home after an unusually complete evacuation of the barium.

The third patient was a plumpish woman of 40 years, who was being examined to exclude malignant disease of the large intestine. The filling of the colon went well but the return through the catheter was poor, and she was sent to the lavatory for evacuation of the enema.

The fourth and last patient was a woman of 65 years who was being given a barium meal and enema in order to confirm an enlargement of the spleen. She was given to drink a mixture of 10 oz. of barium and 2 oz. of water. She drank about 6 oz. of this fluid. She made no complaint and brought back none of the liquid. (There was none of the 'tannic acid" in the drink). She was then given the enema part of the examination, the filling being only as far as the mid-transverse colon. She was turned on her left side and an attempt made to recover the liquid but the return was poor. She was noticed at this time to be 'whoosey' and to respond poorly to requests. She rapidly lost consciousness, respirations became rapid and irregular and she developed convulsions of the limbs. It was thought that the enema had loosened a cerebral or pulmonary embolus. She was returned to the ward, but died 2 hours after the examination.

Meanwhile the third patient had also become ill and it was suspected that the patients had been poisoned by the enemas. She in turn was admitted to the ward and subsequently died 7 hours after the examination.

At autopsy, the appearances were the same in both fatal cases. Well marked cyanosis of the skin with generalized congestion of the internal organs. The lungs were oedematous and plum coloured with subpleural

haemorrhages. There were well marked subendocardial haemorrhages on the septum of the heart (Figs. 1 and 2) and barium emulsion in the intestine. On spectroscopic examination gross methaemoglobinaemia was present in both cases (Fig. 3).

Histology was not helpful and showed congestion throughout the internal organs with no specific changes. One case showed areas of intra-alveolar haemorrhage.

Fig. 1. Subendocardial haemorrhages in the first fatal case.
Fig. 2. Subendocardial haemorrhages in the second fatal case.

Death was due to poisoning by the developer metol hydroquinone.

Following the post-mortem examinations, chemical analysis was carried out on the contents of the sandwich tin and the remaining barium mixture with the following results:

Sandwich Tin:

Total weight of contents	345 g.
Metol	19%.
Hydroquinone	74.5%.
Tannic acid	6.5%.

(Ratio of metol to hydroquinone in Ilford I.D. 19 X-ray developer is 1 : 4).

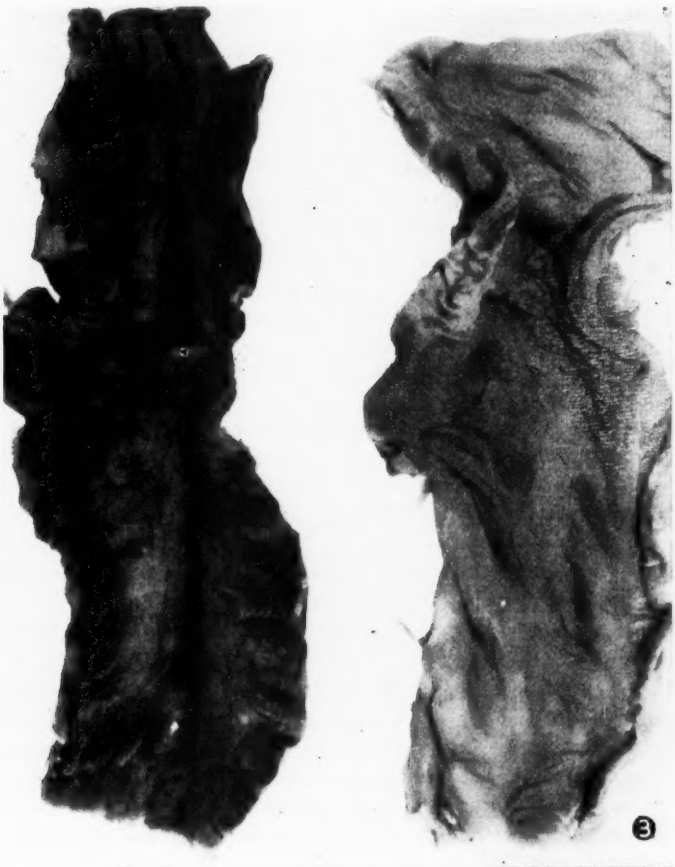

Fig. 3. The sigmoid colon in the 2 fatal cases of metol hydroquinone poisoning, one showing well marked methaemoglobinaemia.

Enema Mixture:

Present largely as oxidation products	Total solids	15.5 g. per 100 ml.
	Barium sulphate (water-insoluble material)	13.8 g. per 100 ml.
	Hydroquinone (ether-soluble material)	1.4 g. per 100 ml.
	Metol	0.3 g. per 100 ml.

Thus it was concluded that:

1. The contents of the tin when received consisted of a mixture of metol and hydroquinone in approximately the same proportion as developer with a small quantity of tannic acid.

2. The enema solution contained no tannic acid.

3. The amount of developer in the tin was approximately that which would be contained in a full packet less that removed to prepare the enema and that sent for analysis.

Following these tragic events the first and second patients were visited at their homes.

The first had no ill effects and refused to come into hospital.

The second felt perfectly well until 8 hours after his enema, when he developed colicky lower abdominal pain which kept him awake all night and he passed 4 loose stools, the colour of which he did not notice. He was persuaded to come into hospital 24 hours after the barium enema.

On admission he was feeling fairly well but had cyanosis of the tips of his nose and ears. There were no abnormal physical signs except tenderness in the right hypochondrium. Spectroscopic examination of the blood was normal.

Thereafter he developed increasing jaundice and progressive anaemia with the haemoglobin falling to 41% (6.1 g.) and reticulocytes rising to 10%. Serum bilirubin rose to 5.0 mg. per 100 ml. The urine contained bile pigments and urobilinogen and the Jaffe test for indican was positive. Liver function tests were normal.

During the first 4 days of his illness the urine was a reddish-brown colour, gradually changing to dark brown.

He was treated with blood transfusions and recovered 4 weeks after the enema.

The sequence of events is difficult to explain. Tannic acid does not spread well when mixed and it is found that the first patients during a barium enema session do not get as much as the later ones. Metol and hydroquinone are only slowly soluable in water (5% at room temperature), and it may well be that very little had dissolved for the first 2 patients.

How the developer came to be in the sandwich tin remains a mystery. Investigation at the hospital was carried out without success. No developer was thought to be missing, although the X-ray department was used on occasions for the private developing of films.

Discussion

These 3 cases of metol and hydroquinone poisoning correspond to the findings in cases reported of poisoning in humans and experimental poisoning in animals.[5, 10]

This latter has been divided into acute, subacute and chronic stages.

The acute stage is characterized by increased sensitivity to stimuli, dyspnoea, hypothermia, reticulocytosis and leucocytosis.

During the subacute stage there is also dyspnoea and hypothermia with haemolytic icterus and alterations of muscle tone.

In the chronic stage there is a progressive anaemia without jaundice, reticulocytosis and profound cachexia leading to death.

Four fatal cases of poisoning by a mixture of hydroquinone and metol have been reported. One of these[9] was accidental poisoning following a barium enema examination containing photographic developer. Fifteen minutes after the enema the patient had convulsions, loss of consciousness with dyspnoea, irregular rhythm of the heart and cyanosis, and died 1½ hours after the enema.

Two were cases[14] in which two men took 15 g. of a mixture of hydroquinone and metol in mistake for Epsom salts. The main clinical symptoms were severe diffuse abdominal pain, haemolytic anaemia and jaundice, with cyanosis, tachycardia, melaena and haematuria. The first case died 75 hours and the second 92 hours after taking the poison, the main post-mortem findings being engorgement of the splenic pulp, phagocytosis of erythrocytes in spleen and liver, marked nephrosis and heavily pigmented casts in the kidney and bile pigmentation of the liver. One of the cases showed an acute myocarditis.

The fourth case[4] was a female, aged 24 years, who swallowed 6 g. of hydroquinone and 2 g. of metol and died 6 days later. Again the clinical features were haemolytic anaemia with cyanosis, jaundice and hypotension. The urine was brownish-black after exposure to air. Post-mortem examination showed bronchopneumonia, pulmonary oedema and reddish-brown urine with fatty degeneration of liver and kidneys and acute myocarditis.

Two cases of hydroquinone poisoning have been reported.

The first,[12] a female aged 36 years, who recovered after taking 12 g. of hydroquinone. She developed tinnitus, sleepiness, suffocation and a swollen tongue. Signs included dyspnoea, cyanosis and drowsiness. The urine was black for the first 4 days and tests for phenol were positive. The blood showed hypoglycaemia and hypercholesterolaemia.

The second case[7] was a negress who committed suicide by swallowing a mixture of 5 g. of hydroquinone and 4.5 g. of benz catechine. During the first 24 hours she had convulsions with loss of consciousness and vomited

black material. The urine and stools were black. At the end of the fourth day there was an icteric tinge of the conjunctivae and the urine contained bile pigment, bile salts and haemoglobin. She died on the 12th day and post-mortem examination showed petechial haemorrhages on the mucosa of gastro-intestinal tract, haemorrhagic infiltration of the perilobular regions of the liver and biliary pigmentation of the parenchymal cells.

One non-fatal case[13] of pure metol poisoning has been reported of a man, aged 33 years, engaged in the manufacture of metol, who presented with black urine, cyanosis and mahogany-brown hands and nails. The urine became clear in 2 days, but the cyanosis persisted for 16 days. Methaemoglobin was present 35 days later.

The mode of action of metol and hydroquinone is not clear. They are both reducing agents and there is evidence to suggest that hydroquinone produces its toxic effects after being oxidised to the more irritant quinone which is associated with colour development.[4]

Methaemoglobin does not appear to be found in any great quantity during life but appears rapidly after death. On this basis the assumption of death from methaemoglobin asphyxia is not tenable.

Haemolytic anaemia and jaundice has occurred in all the cases.

Reported cases of dermatitis due to metol appears to be due to N.N.-dimethyl paraphenylenediamene present as an impurity.[6, 13]

Traumatic Rupture of the Rectum during Administration of a Barium Enema

A man aged 73 years, who had enjoyed good health until 2 years before his death, when he suffered from prolapsed piles, was sent to hospital for investigation of rectal haemorrhage and treatment of his piles.

Eleven days later it was decided to carry out a barium enema examination as an out-patient. The catheter tube was inserted by a staff nurse with slight difficulty which was expected on account of his piles. The tube was passed to the required length and could be seen on X-ray. Barium was injected by gravity from a height of 34 inches and the patient complained of pain which was taken for the normal discomfort during this procedure. On taking the X-rays the radiologist noticed that some barium had spread 4 to 5 inches outside the rectum and it was suspected that the large bowel had been perforated (Figs. 4 and 5).

He was admitted to the ward and the same evening a laparotomy showed barium in the peritoneal cavity and mesentery and a colostomy was performed. He only partially recovered from the anaesthetic and died 16 hours after the operation.

At post-mortem examination he was found to be a fairly well nourished man with some loss of flesh. The rectum (Fig. 6) was found to have a fold

of prolapsed mucosa with internal haemorrhoids and thickening of the wall. In its lower portion there was a small perforation with extravasation of barium upwards around both kidneys (Fig. 7).

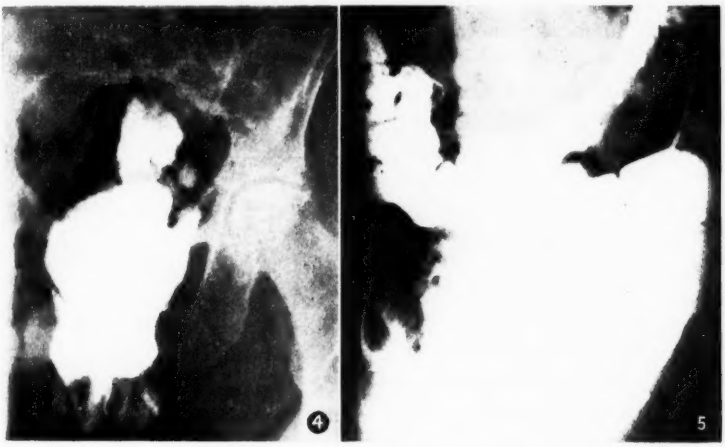

Fig. 4 and *Fig.* 5. X-rays showing the spread of contrast media outside the rectum and the sigmoid colon.

Examination of the other organs showed senile degeneration with atheroma of the cerebral and coronary arteries, infarction in the right kidney, enlargement of the prostate gland and a large hydronephrosis of the left kidney. There was also a small hiatal hernia.

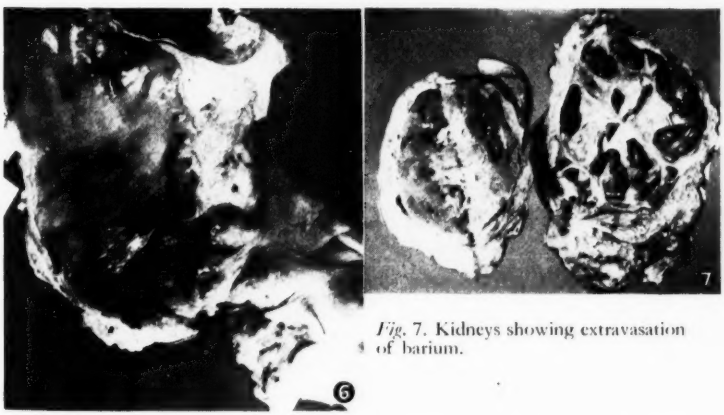

Fig. 7. Kidneys showing extravasation of barium.

Fig. 6. The rectum with prolapsed piles and mucosa with perforation and spread of barium through the subcutaneous tissue.

Death was due to shock due to retroperitoneal extravasation of barium from perforation of the rectum during administration of the barium enema.

Discussion. There are many reports of perforation of peptic ulcers during barium studies. These patients have usually recovered.

There are also several reports of colonic perforations due to pneumatic pressure, proctoscopy and saline and soapsud enemas.

Kleinsasser and Warshaw[8] report a case of perforation of the sigmoid colon during the course of a barium enema for diverticulitis, with spread of the contrast media throughout the abdominal cavity. Their patient recovered after a stormy illness marked by repeated occurrences of obstruction of the small intestine. They draw attention to the fact that their patient received cleansing enemas but did not perforate and query whether these weakened the bowel or whether the added pressure caused by barium as opposed to water played some part in the perforation.

They quote cases of perforations of the rectum and sigmoid colon due to ordinary enemas, water hydrant injuries, proctoscopy and barium sulphate enemas. The mortality proved to be high with these cases.

Bullon and Goldbloom[2] report on serious injuries to the rectum from improperly administered enemas. They felt that there were two factors involved, the hard nozzle of the enema tip and the hydrostatic pressure of the administered material. They also point out that injury to the insensitive rectum will cause little pain.

Burt[3] determined the amount of pressure that the bowel could withstand before rupture by *in vitro* studies. He found that the outer 2 coats rupture first in a longitudinal direction and the mucosa would herniate through this aperture. Then on increasing the pressure still further the mucosa would perforate. He found that the average pressure before rupture of the outer 2 coats was 18 cm. Hg and to perforate the mucosa 21 cm. Hg.

In the case we have described the enema was given from a height of 34 inches, so the pressure at the tip of the tube would be about 7.5 cm. Hg, which is well below Burt's figures.

Pratt and Jackman[11] report 30 cases of perforations of the rectal wall by enema tips. Eight of these were intraperitoneal perforations and 50% died. They caution against inserting the enema tip more than 2 inches into the rectum and pointed out that rupture usually occurs in the anterior wall of the bowel. They properly advise early operation with closure of the perforated bowel.

Andressen[1] was able to accumulate 46 cases of perforation during proctoscopy. His findings indicated that after 6 hours the mortality rate doubled and that after 12 hours it trebled. Sudden severe pain occurred in 55% of the patients; 34 were operated on with 11 deaths (32% mortality), and

12 were not operated on with 8 deaths (66% mortality). In those who were operated on immediately there was only an 8% mortality.

Survival after perforation of the large intestine is rare, whereas after perforation of peptic ulcers it is common. It seems reasonable to suppose, supported by experiments on dogs,[8] that this is merely due to the difference in bacterial contamination in these cases.

Death from Shock and Chemical Peritonitis Following Administration of a Barium Enema into the Vagina

A woman aged 56 years, married but with no children, was admitted to hospital for anaemia. She had been treated with iron injections. Examination of the faeces showed persistent occult blood, the source of which had not been ascertained by barium meal, although post-mortem examination later suggested that this might have been due to a hiatal hernia. It was decided to carry out a barium enema to exclude malignant disease of the large intestine and this was performed 13 days after admission.

In view of the patient's age, it was decided to use a retaining catheter with a balloon attachment of the St. Bartholomew's Hospital type (Fig. 8). When this was inserted by the radiographer, the patient complained of pain and discomfort and repeated several times, 'Please not again', but as the introduction of the device, especially after repeated preparatory wash-outs, produces some discomfort in the majority of patients, this was not considered abnormal. This patient had previously been given 4 separate wash-outs by a nurse in order to prepare the colon for the barium enema. During these preparatory enemas no difficulty had been experienced in inserting the catheter and the patient had not complained of pain. They had produced a normal faecal result, the fourth being clear, and no haemorrhage had occurred and no blood had been seen in the returned fluid.

After insertion of the barium enema catheter, the filling of the balloon with air did not markedly increase the patient's discomfort. The barium was then administered but there appeared to be an obstruction which, on screening, was confirmed by a small collection of barium, presumed to be in the rectum, with a complete obstruction at what was thought to be the sigmo-rectal junction (Fig. 9).

After the examination the patient was put on the bedpan for 5 minutes, the balloon was deflated and the catheter removed after 2 minutes. The catheter was found to be blood-stained and blood was found in the barium passed.

Within 15 minutes of return to the ward she was found to be in a shocked condition and bleeding profusely from the vagina. A blood transfusion was started and the vagina packed after rupturing an intact hymen.

The following morning her general condition appeared improved but the pulse was still 120 per minute and the blood pressure 70/40 mm. Hg. There was no abdominal rigidity, distension or tenderness.

By lunch time, however, she had deteriorated, the abdomen was tender and silent and paralytic ileus was diagnosed. She was seen by a surgeon who decided on a laparotomy. By this time, radiologically, it was clear

Fig. 8. Self-retaining catheter of type used for enema.

Fig. 9. X-ray taken at time of examination with catheter *in situ*.

that barium was free in the peritoneal cavity (Fig. 10). The operation showed peritonitis due to barium and as it was believed to be due to perforation of the growth a colostomy was performed. As there was bleeding from the vagina, the hymen was incised and with difficulty it was possible to see a vaginal tear about 1½ inches long. On rectal examination nothing abnormal was found. There was no growth, no blood and *no barium.*

She was treated with blood transfusions and a noradrenaline drip, but although she recovered from the anaesthetic she died 8 hours after the operation.

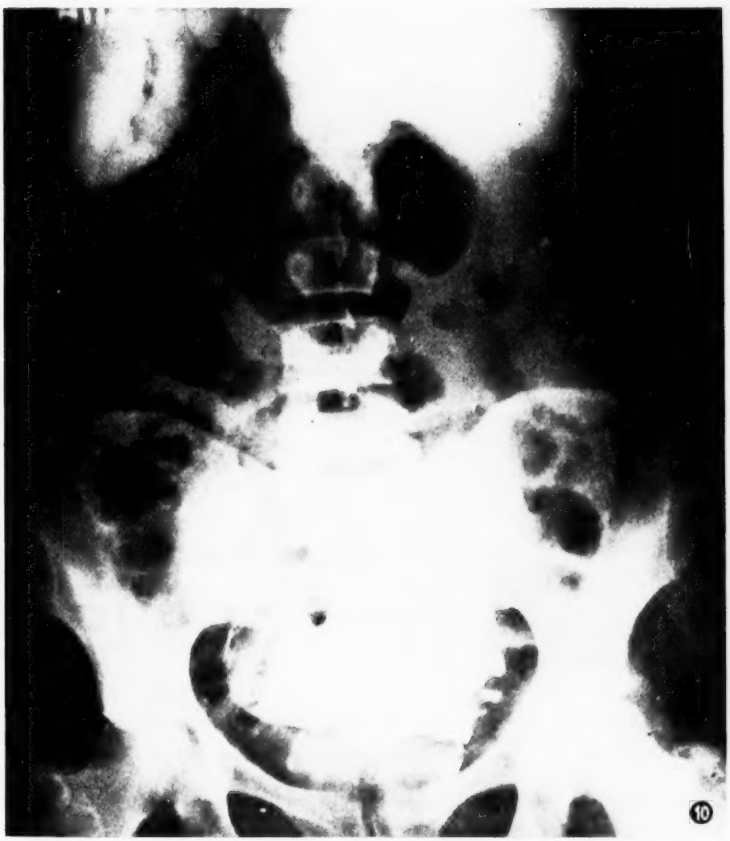

Fig. 10. X-ray taken the day after the enema.

At post-mortem examination she was found to be a somewhat thin woman with an operation incision in the lower abdomen for laparotomy and left iliac colostomy.

The intestines were somewhat dilated and there was an extravasation of blood extraperitoneally in the loose pelvic tissues extending from the broad ligament to the pubis, which was more marked on the right side.

A tight hymen had been incised at operation and on each lateral wall of the vagina there were tears in the mucosa due to overstretching with involvement of the underlying tissues where barium had penetrated. This was more marked on the right than on the left.

There was considerable congestion of the Fallopian tubes, particularly at their distal ends, and on dissection barium could be demonstrated. On opening the uterus a thin layer of barium could also be demonstrated and this is well seen in the X-ray photographs taken before and after death. There was no evidence of a lesion in the rectum nor was any barium present (Figs. 11 and 12).

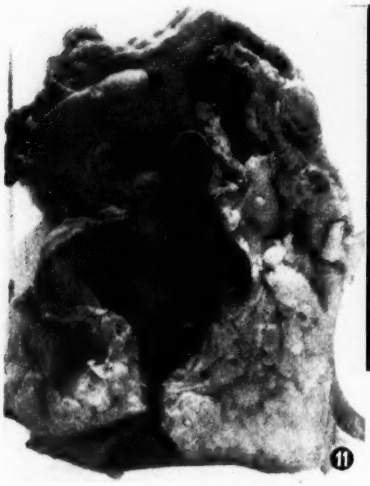

Fig. 11. Post-mortem specimen of the vagina and the uterus, showing the tears in the lateral walls of the vagina.

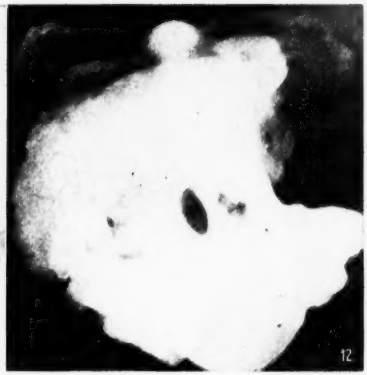

Fig. 12. X-ray of the post-mortem specimen, showing the extravasation of barium through the Fallopian tubes.

The stomach was slightly dilated and contained fluid contents. The lower 3 inches of the oesophagus showed granularity of the mucosa which was congested with one or two dilated veins. There was a hyperaemic area at the cardiac end of the stomach.

The heart showed coarse subendocardial haemorrhages on the septum (Fig. 13).

Fig. 13. Heart showing subendocardial haemorrhages.

Discussion. From the post-mortem findings, supported by the ante-mortem radiological appearances, it is clear that the vagina had been dilated, presumably by the inflated balloon, and the introitus completely obstructed. The resultant flow of barium under gravity pressure had been forced through the uterus and Fallopian tubes into the peritoneal cavity and also through the tear in the vaginal wall, leaving a deposit. The subendocardial haemorrhages suggested a severe drop in blood pressure.

A search of the literature does not reveal any similar cases. The sequence of events, however, is quite obvious and to be expected once the initial mistake of inserting the catheter into the wrong orifice is realized.

Summary

Three types of therapeutic accidents occurring during radiological procedures are described. Two of these seem to be avoidable.

Our thanks are due to Sir William Bentley Purchase, *C.B.E., M.C.*, H.M. Coroner of the County of London, for allowing us to have and use the Notes of Evidence on the Inquests of these cases; and to Mr. A. Hardy of this Department for the photographs.

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Therapeutic Accidents

Mr. J. P. Reidy

Gentlemen: I came here to-day not with the idea of reading you a paper but to show a few slides. These I thought might be of interest to you showing conditions which reach us as clinicians and may not reach you as pathologists.

I was reminded of the story about 'the moment of truth' which, of course, comes to us all when we are faced with a decision. Some of us recognize it at operation when we have gone so far and find an inoperable carcinoma; and there is also a point of no return—rather like that experienced by the airline pilot in mid-Atlantic. The pathologists recognize it as accessories after the fact at autopsy and they recognize the moment of truth that may or may not have come to the clinicians in their treatment of the case.

'Moment of truth' can be used in another context as judgment. If one is a good clinician one recognizes the moment of truth before one embarks on the treatment—that is called good judgment; but there is many a slip before the recognition of the moment of truth.

I feel that these therapeutic accidents could be classed under therapeutic, radiological and surgical, and we have heard this morning how accidents might happen by use or misuse of drugs or by normal use of drugs plus idiosyncrasies of patients often brought to light in their reactions to these drugs.

Injections of Dindevan. A female patient had Dindevan injections. The thigh developed massive skin necrosis overlying intense haemorrhages in the leg muscles. She survived and is going home soon following excision of the slough and cover with skin grafts.

I saw another case 2 years ago when the haemorrhage was so massive that the woman died.

There is another therapeutic case of a child brought in 3 weeks before with meningococcal septicaemia. The houseman put up a drip in the right calf. After 2 or 3 minutes the calf was seen to swell visibly, so the drip was disconnected and put into the other leg. Subsequently, there was widespread necrosis of skin and muscles of the lower leg, necessitating a below-knee amputation.

Radiological catastrophies come frequently in plastic surgery, and they probably do not reach the pathologist at all. The common one, of course, is where the fond mother of 30 years ago takes her daughter of 17 to 18 to a

radiotherapist to have a few hairs removed from the upper lip. Some 30 or 40 years later the girl, now a full grown woman, presents with carcinoma of the upper lip requiring treatment. Nowadays we are in a very much happier position, and the machines are vetted by a physicist and the dose is more accurate than it was 30 or 40 years ago. However, there is still a difference of opinion between surgeons and radiotherapists whether radiotherapy is better alone or surgery alone, or whether a combination of the two is the ideal.

Maldevelopment Occurring in a Boy from Radiotherapy thought to be of a Correct Dosage. A boy now 18 years of age had a naevus on the left side of his neck which was radiated with the result that the sternomastoid muscle and other muscles of the left neck failed to develop. He has a large scar contracture down the side of the neck. There is maldevelopment on the left side of his skull, and his eyes are on different levels. Clinicians fail sometimes to realize that radiation has a most profound effect on growing children, and the result is often worse than the disease.

I nearly joined the ranks of those who appear in Court when some years ago I injected a large cavernous naevus of the face in a girl. I injected sodium morrhuate, about 40 c.c., and she lapsed into a coma and remained so for 10 hours. I thought I would have to appear in a Coroner's court to explain the origin of cavernous sinus thrombosis. Happily, however, she recovered and some months later she returned and I completed the treatment. 'There but for the Grace of God', one would say.

Radiation Necrosis. The upper arm and the right shoulder and breast in the next case underwent radiation necrosis following radical mastectomy for carcinoma of the breast. Examination of the specimen after operation showed that it was not a carcinoma at all, but a simple growth. However, she had a heavy radiation, with the typical result of X-ray burns. Fibrosis in the axillary region with blocking of the lymphatics produces an arm about the size of an ordinary thigh. This shows the effect of radiation given with judgment and skill.

The next case is that of a man with carcinoma of the floor of the mouth. The growth was believed inoperable, and so a very heavy dose of radiation was given. Inevitably, gross sloughing took place of the floor of the mouth and of the submental skin. It will be appreciated that in some cases of inoperable carcinoma there has to be heroic over-dosage of radiation in order to give the patient a chance of survival.

Lastly, there are the results of surgery and there are the treatments for the relief of surgery previously perpetrated, and I mentioned earlier that patients have idiosyncrasies to drugs. There are also the idiosyncrasies of physicians and surgeons which are just as much to blame as those of patients. The surgeons in particular have blind spots in their mental equipment. There is the type of surgeon who can do everything. He is not put off by a case

he rarely sees or has never treated. A common example is the case that has been treated by a general surgeon for repair of the cleft palate. Those who have heard speech from a badly repaired cleft palate will know what I mean. One can control herniae with trusses; one can hide wooden legs; some may even wear 'falsies' without notice; but one cannot disguise one's speech, and a child's progress may be wrecked where inadequate surgery has been performed by one who has no skill.

The last case is that of a man with a pressure sore where an attempt has been made to rotate a skin flap on the back to cover the defect. The flap separated, since it was not correctly designed and was under tension. The patient is doubly worse off because he has lost good skin and needs another graft.

Discussion

Dr. Camps: We have seen the things that ought to have been done and ought not to have been done and things not done too well. I think it is interesting to hear from Mr. Reidy that surgeons still have consciences. Now we have some 20 minutes when I shall invite one or two to open the discussion.

Dr. Obersteg: In our country we have not many cases. We have air embolism, and embolism from pneumothorax, air embolism with blood transfusion under pressure, but in the last 5 years in Basle I have had only 2 or 3 cases of medical misadventure.

Dr. Imrie: A common problem as far as I can see is when a person has been treated, where does the responsibility lie. I have a case in mind where a boy died after having his tonsils removed and later developing multiple abscesses in his lungs under the care of his general practitioner. He was then sent into another hospital where he died. The question here is where one attaches responsibility—the surgeon who removed the tonsils or the doctor at home who had not thought of the possibility of such a disease, and in that case it was rather difficult to know where to attach the blame.

Air-Comm. Stamm: I had an interesting case of a lady whose husband had served in the tropics some years before and suffered from kala azar. She presented with a lesion of the vulva and the husband's brother, who was a doctor, saw her and had her Wassermann reaction done. This came back as a weak ? positive. On the strength of this, instead of having this treated, the case was rather peculiarly handled and the brother of the husband refused to have her treated by him and transferred her to another doctor. She was labelled as a syphylitic and treated as such and her husband left her. Some 6 months later when the treatment had had no effect, and after passing through various hands, a biopsy was taken and it was found that she had kala azar. Incidentally, her husband then returned.

I speak as a pathologist who is rather more clinical than forensic and one thing that has struck me is the emphasis you put on who should pay for the damage and who is responsible rather than how can we stop it from happening again. My interest is preventive rather than compensatory. I think a tie-up between forensic pathologists and clinicians could be very beneficial. We have had a paper this morning on over-dosage. I think we should have a paper sometime on under-dosage. When antibiotics came in it was well known that we could produce resistance. One particular case that illustrates my point on under-dosage is again kala azar. A patient in Palestine was treated for this and he only got half way through his treatment. He came back home considered as a treated case, had a relapse and was again treated but by that time he was resistant to treatment. He had had something like 16 to 18 treatments after a period of 10 years and finally died. That was a case of under-treatment.

We have come across lately some renal deaths where, by the time they come to us to be treated on the artificial kidney, they have very elevated proteins and calcium because people have been pouring in physiological fluids. I think I have seen more therapeutic deaths from fluids being put into patients—just plain drowning—because people have been putting in far more fluids than the poor patient can take.

Another point in relation to new drugs is that when a research team produces a new drug, very often the new drug precedes the skill of the local laboratories. It should be controlled by new techniques.

People have talked about death from wrong labelling. We know well the one from blood transfusion: two patients with the same name from the same ward, etc. In this case the mistake comes to light dramatically. I often wonder how many patients have died from mistakes that are not so dramatic. I have seen in the last 4 years 3 cases where a biopsy specimen has arrived from the surgical theatre and has been wrongly labelled. These came to light because the sex was wrong. We had a testis from a Mrs. X and it then became clear that another specimen from another theatre belonged to Mrs. X and the testis belonged to Mr. Y. One wonders in a case, like the one Mr. Reidy mentioned of the breast carcinoma which was not in fact carcinoma, how many of these cases have been operated upon where the biopsies are wrong.

Notes and News

Post-Graduate Course in Criminology in the University of Cambridge

University of Cambridge: Institute of Criminology

The University of Cambridge has established a Post-graduate Course in Criminology, to be given by the Institute of Criminology. The first course will commence on 1 October 1961. It will be held during the three terms of the academic year and will end in July 1962.

A Diploma in Criminology will be awarded by the University, to those who have diligently attended the course, and who, at its completion, have successfully passed a written examination in five papers covering the subjects prescribed for the course.

The Programme of Teaching will consist of lectures, seminars and practical work: 105 lectures and 90 seminars will be given, dealing with all the major aspects of criminology, with particular reference to the development of criminological and penological thought and practice; the methodolgy of criminological research; the psychological and psychiatric context of criminal conduct; the sociology of crime; the principles of criminal law and procedure; the sentencing process, and the effectiveness of punishment and other methods of treatment; the non-institutional and institutional treatment of juvenile, young adult and adult offenders; and certain aspects of the prevention of crime.

Practical Work, during vacations as well as term time, will be undertaken by the students, at penal and psychiatric institutions, probation and after-care centres, and other agencies concerned with the prevention of crime and the treatment of offenders. Individual work will be required at the seminars; and the International Library of Criminology of the Institute will be available to those who attend the course.

Instruction will be given by the Wolfson Professor of Criminology; by the Senior Staff and Visiting Fellows of the Institute; by other members of the teaching staff of the University of Cambridge; by visiting lecturers; by experts from the Home Office and the Home Office Research Unit, and by others with particular experience in the administration of criminal justice.

Admission to the course will be open to those who already hold a university degree in any subject, not necessarily in law. In very exceptional circumstances, candidates who do not hold a university degree may be considered for admission, if they have either made an important contribution

to criminology by research or gained outstanding practical experience in administration. The number of admissions in any one year will be limited in order to maintain the highest possible standard. Those admitted to the course will be made members of the University, and will be expected to seek admission to a college.

Application Forms for Admission to the post-graduate course are available from the Secretary, Institute of Criminology, 4 Scroope Terrace, Cambridge, England. The completed forms, together with evidence of necessary qualifications, must reach the Secretary not later than 15 March 1961, for the course commencing in October 1961.

Book Review

FORENSIC MEDICINE: TEXTBOOK

Forensic Medicine: Observation and Interpretation. By A. Keith Mant, M.D. (Lond.). (1960. Pp. 257 + Index. With 118 Figs. 42s.). London: Lloyd-Luke (Medical Books) Ltd.

This book was written mainly to assist doctors and others whose task it is to make a preliminary examination of the body and surroundings at the scene of violent or sudden deaths.

It should achieve success in this object, as most of the common circumstances of homicide, suicide, accident and sudden deaths from natural causes are properly dealt with, and amply illustrated by the author's case records and photographs. There is, throughout the book, a commonsense approach to the problems likely to be encountered and in general the opinions offered on the external pathological findings in such cases are sound.

It would have been worthwhile to warn doctors, in describing their duties at the scene of crime (pp. 10 and 11), that they should do nothing until photographs have been taken, except in those rare cases in which resuscitative measures are indicated. Also in discussing the findings in deaths from mechanical obstruction of the airway, the author seems to suggest that the absence of any of the 'general' signs of asphyxia (cyanosis, petechial haemorrhages, etc.) is due to an early termination of the process of obstruction by death from reflex cardiac arrest. Many pathologists would not like to draw this inference. These are minor details. The general approach is sound.

The book concludes with a short section on the medico-legal aspects of sexual offences.

The volume will be of great value to those (police surgeons, Coroner's Officers and C.I.D. officers) for whom it was written. It is probably not quite comprehensive enough for medical students studying Forensic Medicine in some medical schools. Its value for the forensic pathologist will be mainly in the interesting case summaries, which are always of value when similar cases are encountered.

CORRESPONDENCE

Alcohol Ingested by an Individual

To the Editor: I have read with interest the article on the *Simple Determination of the Amount of Alcohol Ingested by an Individual* in your *Journal* (1960, Vol. 7, No. 2). While in full agreement that the Table permits rapid determination of the minimal quantity of alcoholic drinks an individual must have taken, there are a few points to which I should like to draw attention.

In the formula for calculating absorbed alcohol (p. 170) an arbitrary figure of '0.1% alcohol in the blood' is used. If this were a w/w figure, i.e. 0.1 g. alcohol per 100 g. blood, then the formula would be correct. But unfortunately this is a w/v figure denoting 0.1 g. alcohol per 100 ml. blood and hence the average specific gravity of blood[1] (1.054) should be taken into consideration.[2] The figure in question thus becomes:

0.1 g. alcohol per 105.4 g. blood or 0.0949 g. alcohol per 100 g. blood.

This means that the figures for *Total Amount of Alcohol in the Body (in Millilitres)*, as given on pp. 109–111, are approximately 5% too high.

The author of the article referred to is to be commended for creating a comparatively simple formula which can be applied in countries using British weights and measures.

References

1. Harrison, G. A. (1937): *Chemical Methods in Clinical Medicine*, p. 336. London: J. and A. Churchill, Ltd.
2. van Gent, P. K. (1957): S. Afr. Med. J., **31**, 1304.

P. K. van Gent.

Government Chemical Laboratories,
Port Elizabeth.
16 September 1960.

Andrew Campbell Watt Memorial Fund

To the Editor: A Memorial Fund has been started to commemorate the late Dr. Andrew Campbell Watt.

The following have agreed to serve as the Trustees of the Fund:

Mr. Keith Allen	Dr. S. Jacobson
Dr. Allan Bird	Mr. R. Krynauw
Mr. R. Bird	Mr. C. W. Law
Prof. I. W. Brebner	Mr. I. A. Maisels, Q.C.
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Mr. J. A. Douglas	Mr. H. Mendelow
Dr. N. E. C. de la Hunt	Mr. J. N. MacKenzie
Dr. J. C. Gilroy	Mr. R. B. Sinclair

Prof. Norman Dott will represent Trustees in United Kingdom.

The Fund is to finance a scholarship to assist deserving South African graduates in medicine to study neurology or neuro-surgery.

The Trustees are confident that the generosity of his friends will ensure an amount which will allow this to be carried out on a substantial scale.

Should the amount collected fall short of the sum necessary to establish a Scholarship, it is hoped to finance an annual lecture in his memory.

The Trustees feel that medical practitioners in South Africa would wish to be informed of the establishment and objects of this Fund, and that they might wish to make some contribution. Those who care to assist in making this Memorial a reality, should send their contribution to the Honorary Treasurer, R. B. Sinclair Esq., c/o Douglas Low & Co., Aegis Building, Johannesburg. This will be most gratefully received and acknowledged.

Johannesburg. The Trustees.